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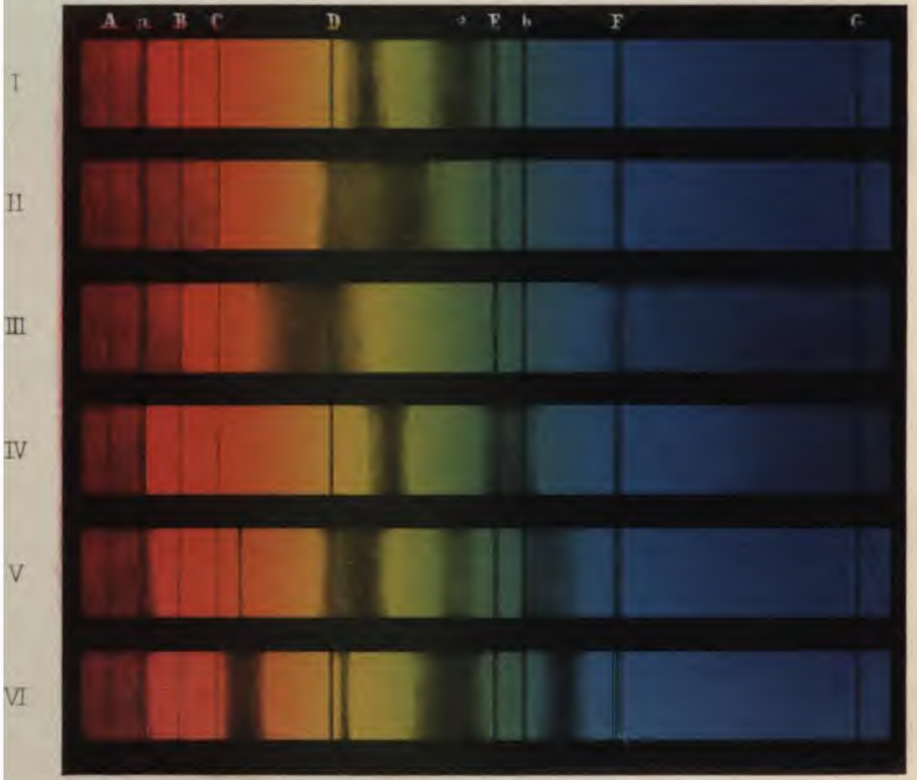

ABSORPTION SPECTRA OF BLOOD.

I. —— *Oxyhaemoglobin.*
II. —— *Reduced haemoglobin.*
III. —— *Alkaline haematin.*
IV. —— *Haemochromogen (reduced haematin).*
V. —— *Haematoporphyrin in an alkaline solution.*
VI. —— *Haematoin (allied to acid haematin).*

Mintern Bros. Chromo lith.

THE ELEMENTS OF
PHYSIOLOGICAL AND PATHOLOGICAL
CHEMISTRY.

A HANDBOOK FOR MEDICAL STUDENTS AND PRACTITIONERS

CONTAINING A GENERAL ACCOUNT OF

NUTRITION, FOODS AND DIGESTION, AND THE CHEMISTRY OF THE TISSUES, ORGANS, SECRETIONS AND EXCRETIONS OF THE BODY IN HEALTH AND DISEASE,

TOGETHER WITH THE METHODS FOR PREPARING OR SEPARATING THEIR CHIEF CONSTITUENTS, AS ALSO FOR THEIR EXAMINATION IN DETAIL, AND AN OUTLINE SYLLABUS OF A PRACTICAL COURSE OF INSTRUCTION FOR STUDENTS.

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WITH EVERY FEELING OF ADMIRATION AND FRIENDSHIP

TO TWO OF THE AUTHOR'S FORMER TEACHERS,

DR. FELIX HOPPE-SEYLER,

The distinguished Professor of Physiological Chemistry in the University of Strassburg,

WHOSE NAME IS SO OFTEN QUOTED IN THE FOLLOWING PAGES,

AND

DR. JOHN SYER BRISTOWE, F. R. S., LL. D., F. R. C. P.,

Senior Physician and Lecturer on Medicine at St. Thomas's Hospital,

FROM WHOM HE HAS RECEIVED SOME OF HIS BEST LESSONS

IN MEDICINE.

PREFACE.

It is unnecessary at the present day to insist upon the importance of a knowledge of chemistry, and particularly of physiological and pathological chemistry, to the student of medicine; but it must always be carefully borne in mind that just as the proper study of pathology requires a previous knowledge of histology and physiology, so the study of physiological chemistry should be founded on a well-grounded and extensive acquaintance with the principles of general chemistry. Not, indeed, until a close connection was established between chemistry and medicine did any decided advance occur in the latter; and by its means the medicine of the future will undoubtedly be still further enlightened and extended. Physiological chemistry promises much even in the treatment of disease; for it is beginning to be seen, from the investigation of the molecular constitution of different bodies, that there exists a distinct connection between their specific atomic grouping and their physiological action. And even in some of the most interesting investigations of the pathology of the present day—those connected particularly with the causation of infectious diseases—physiological chemistry will, without a doubt, take a most prominent place; for there is every reason to believe that the micro-organisms which play so important a part in these diseases really act by virtue of a ferment-working virus or zymosis of some kind which accompanies them or is generated by them. The hope may therefore be expressed that the further investigation of the chemical properties of these microzymes and their respective zymoses will shortly lead to a closer acquaintance with their mode of action, as well as to a knowledge of how to stamp them out or to thwart their activity. And either to understand them or to be able effectually to counteract their virulence will demand a great increase upon our present knowledge of the chemistry of the body both in health and disease.

In the following pages an attempt has been made to present the medical student and practitioner with an outline of the most important branches of physiological chemistry; but to render the work more complete, both for private study and for laboratory purposes, I have been compelled to introduce brief descriptions of such bodies as sugars, fats, and certain salts, etc., which are more appropriately treated of in works upon general chemistry.

I have treated my subject under four main heads:—

Book I. *Nutrition and Foods.*
" II. *Digestion and the Secretions concerned.*
" III. *The Chemistry of the Tissues, Organs, and Remaining Secretions.*
" IV. *The Excreta: the Fæces and urine.*

Every effort has been made to render the work as practical as possible. I have accordingly confined myself chiefly to those parts of the subject which bear most directly upon practical medicine; and I feel sure that, by following the indications laid down throughout the book, effectual assistance will often be given to the physician in establishing the diagnosis as well as the etiology of many of the complicated diseases he may be called to treat or investigate.

Temperatures have, with a few exceptions, been stated in centigrade degrees. A choice of methods and processes has generally been given, particularly when there is any difficulty to be overcome; and, when the importance of the subject merited it, not only the methods but also the theories of different authorities have been detailed.

Discussions of unsettled questions have as much as possible been avoided; and, keeping steadily in view the object for which the book is intended, the author has been compelled, and often reluctantly, to omit many subjects and details that in themselves are highly interesting and instructive, but which he deemed beyond the limits of the present treatise. Despite his wishes, however, the book has far outgrown his original intentions.

The urine, as being from a physiological as also a pathological point of view one of the most important excretions of the organism—many of its indications being of the most precious and valuable kind to the physician and surgeon both in diagnosis and treatment—has therefore been treated with considerable detail. Some of the most approved methods for the examination of this fluid have been given, and, as far as possible, all its indications that possess a diagnostic value have been referred to, with a view to establishing as rational a line of treatment as possible.

In the syllabus with which the book concludes a course of procedure is indicated which may be pursued with great advantage by the student; but of course the amount of work to be done will largely depend upon the time at his disposal. Unless, however, this is very limited, it would be greatly to his benefit to go through the scheme I have laid down, omitting possibly a few of the modes of preparation in some of the sections. By means of demonstrations also it would be possible to lighten his labors considerably; and only in this way, it seems to me, will the student be able to grapple successfully with the task before him. But it must be confessed that it is far too commonly the case for students to begin the study of physiological chemistry before having attained any accurate acquaintance with general chemistry. This is greatly to be deplored, for under such circumstances they cannot derive the benefit they otherwise would be sure to gain. Not only should the student have a thorough knowledge of the elements of general chemistry, but it would also favor his progress greatly if, in addition to the ordinary practical course of qualitative analysis generally pursued, he performed a few simple quantitative analyses.

The names of authorities have, as a general rule, been quoted, but references have been entirely omitted, as it was found that the space which would have thus been occupied would have been much too considerable in a mere manual like the present; but while, as far as I possibly could, I have acknowledged in the brackets throughout the book the very numerous authorities responsible for the facts or theories stated, yet I feel that I should at least mention here the works to which I have been particularly indebted, viz.: HOPPE SEYLER'S "Physiologische Chemie" and "Handbuch d. Physiologisch- und Pathologisch-Chemischen Analyse," HERMANN'S "Handbuch d. Physiologie," HOFMANN'S "Lehrbuch d. Zoochemie," KÜHNE'S "Physiologische Chemie" and "Untersuchungen aus d. Physiologischen Institute d. Univ. Heidelberg," SALKOWSKI and LEUBE'S "Die Lehre vom Harn," LIEBERMANN'S "Chemie d. Menschen," PFLÜGER'S "Archiv f. Physiologie," GAUTIER'S "Chemie appliquée, à la Physiologie," PAVY'S "Food and Dietetics," SMITH'S "Foods," FOSTER'S "Physiology," and WATT'S "Dictionary of Chemistry."

CROFTON LODGE, STREATHAM,
LONDON, S.W.:
March, 1884.

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PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY.

BOOK I.

NUTRITION AND FOODS.

CHAPTER I.

APPARATUS AND CHEMICALS.

THE student should be provided with the following REAGENTS:—

Water, rain or distilled.
Alcohol, absolute
methylated spirit.
Ether.
Chloroform.
Glycerin.

Hydrochloric acid.
Nitric “
Sulphuric “
Glacial acetic “
Oxalic “
Chromic “
Tartaric “ (1 : 4).
Tannic “ (1 : 10).

Ammonia.
Caustic potash, in sticks and in solution (1 : 2), and (1 : 8).
Caustic soda.

Slaked lime.[a]
Baryta water (1 : 15).

Alum.
Ammonic oxalate (1 : 20).
“ chloride (1 : 8).
“ carbonate (1 : 4).
“ molybdate.[b]
Bromine.
“ water (1 : 30).
Baric chloride (1 : 10).
“ nitrate (1 : 12).
“ “ (saturated).
Bismuthic nitrate.
Calcic chloride (1 : 5).
“ carbonate.
Chloride of lime.
Copper sulphate (1 : 12).
Chlorine water.[c]
Iodine, tincture.

---

[a] *Slaked Lime.*—To prepare *milk of lime* place some fragments of recently burnt lime in a capsule, and add a little water, stirring the mass with a glass rod. A fine powder will be obtained, when more water is to be added until a milky-looking fluid is obtained, which is to be filtered through some muslin.

[b] *Molybdate of Ammonia.*—Dissolve 4 grams in a little ammonia, and then add about 60 c.c. nitric acid; lay aside for some time, decant, and make up to 100 c.c. with water.

[c] *Chlorine Water.*—Prepare chlorine gas by gently warming some black oxide of manganese with strong sulphuric acid in a small retort, and pass the gas into water to saturation.

Or heat the following mixture: sodic chloride 18, black manganic oxide 15, sulphuric acid 45, and water 15.

Iodine solution (5 grains shaken up with 1 oz. water).[d]
Indigo solution.
Iron sulphate (1 : 4).
" sulphide.
Litmus solution.[e]
Liquor ferri perchloridi (1 : 10).
Lead acetate (1 : 8) (neutral and basic).
Magnesic sulphate (1 : 6).
" " (saturated).
Magnesia mixture.[f]
Mercurous chloride (calomel).
Mercuric chloride (1 : 16).
" nitrate.
Millon's reagent.[g]
Magenta.
Platinic chloride (1 : 10).
Potassic chromate (1 : 20).
" nitrate (free from chloride).
Potassic sulphocyanide.
" ferrocyanide (1 : 12).
" ferricyanide (1 : 12).
" iodide (1 : 20).
Rosolic acid (1 : 100 alcohol).
Starch solution.[h]
Sodic acetate.
" carbonate (saturated and 1 : 8).
" chloride (saturated).
" phosphate (saturated and 1 : 20).
Sodic sulphate (saturated).
" nitroprusside.
" hypochlorite.
Silver nitrate (1 : 30).
Sulphuretted hydrogen and ammonium sulphide.[i]
Tin protochloride.
Zinc chloride.

---

[d] *Solution of Iodine.*—Dissolve 2 parts potassic iodide in 100 parts water, and then add 1 part iodine and shake well.

[e] *Litmus Solution.*—Place 10 grams litmus cake in ½ litre distilled water, leave it to digest in a warm place for 3 or 4 hours, and then decant the clear liquid from the sediment. To half of it add a few drops very dilute sulphuric acid until a faint reddish or violet tinge is obtained; and to the other half a very little dilute alkali until it becomes blue.

[f] *Magnesia Mixture.*—Crystallized sulphate of magnesia 1, ammonium chloride 2, ammonia 4, water 8. Mix well together.

[g] *Millon's Reagent.*—1 part mercury is treated with 2 parts nitric acid (sp. gr. 1·4) in the cold, and then over a water bath till completely dissolved; it is to be diluted with 2 parts water, and the clear liquid decanted after 3 or 4 hours.

[h] *Starch Solution.*—Rub 1 part starch with 8 parts cold water in a mortar; then pour the mixture slowly into 40 parts boiling water.

[i] *Sulphuretted Hydrogen.*—Prepare this when required, using a large wide-mouthed bottle half filled with dilute sulphuric acid. The cork of this bottle is pierced by two holes, through one of which passes tightly a strong glass rod hooked upwards at its lower end. This hook supports a small porcelain dish pierced with holes, and in which fragments of ferric sulphide are placed. The other hole in the cork contains the tube for the escape of the gas, and to this is fitted a wide drying tube filled with cotton. When the gas is needed, lower the ferric sulphide into the acid by pushing down the supporting rod; by raising it again the evolution of gas ceases. It is advisable to wash the gas by passing it through a little water.

Ammonic Sulphide.—Prepare this by saturating, say, 60 c.c. liquor ammoniæ with hydric sulphide gas, and adding to it 40 c.c. more of the liquor ammoniæ.

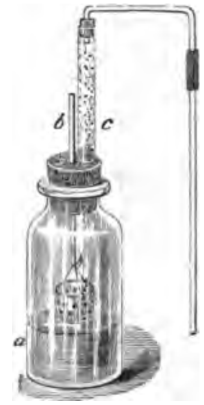


FIG. 1.—SULPHURETTED HYDROGEN APPARATUS. *a*, large bottle containing dilute sulphuric acid; *b*, a glass rod that can be moved up and down in the cork stopping the bottle, and supporting a small porcelain cup pierced with holes and filled with ferric sulphide; *c*, a drying tube filled with cotton.

Of APPARATUS it is well to be provided with the following:—

Test tubes (12).
Test-tube rack with draining pegs.
Small funnels (½ oz., 2 oz., 4 oz., 8 oz., 10 oz.)
Small tube funnels.
Glass rods.
“ tubing of different diameters.
Wash bottle (water).
“ (spirit).
Two or three nests of beakers.
Flasks of different sizes, including Florence flasks.
Porcelain evaporating dishes.
Small conical glasses.
Watch glasses.
Water bath.
Sand bath.
Spirit lamp.
Bunsen lamp.
Rose or ring burner.
Blowpipe.
Three-cornered and rat-tailed files.
Cork-borers.
Spatulas—one of platinum.
Crucible tongs.
Wire triangles.
Retort stands provided with rings of different sizes.
Pincers.
Forceps.
Woulf's bottles.
Wedgwood mortar (1 pint).
Small mortar.
Platinum foil.
“ wire.
Small porcelain crucibles.
“ distillation apparatus.
An air bath.
Thermometer indicating up to 150°
An ordinary balance.
A chemical balance.
India rubber tubing.
Sheet india rubber.
A microscope.
A polariscope.
Slides and cover glasses.
Urinometer.
Pipettes.
Graduated pipettes.
Glass measures.
A set of Mohr's burettes.
Filtering paper.
Blue and red litmus paper.
Litmus solution and cake.
Slips of paper prepared with acetate of lead, turmeric, and ammonium molybdate.

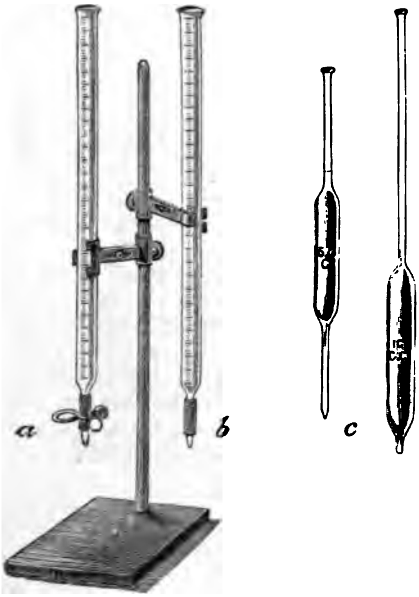
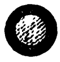


FIG. 2.—MOHR'S BURETTES AND PIPETTES.
a with a pinch cock, b with a piece of glass rod inserted in the india rubber connecting tube; c, pipettes for delivering definite quantities of liquid.

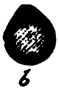
Pipettes are glass tubes graduated so as to deliver exact quantities of liquid, as, say, 5 c.c., 10 c.c. and 50 c.c. respectively. They are inserted into the liquid, and this is sucked up till it nearly fills the pipette; the upper end is then rapidly covered with the tip of the forefinger, and the liquid allowed to escape by cautiously raising the finger until the level of the liquid is opposite the graduation mark desired.

Burettes.—Three Mohr's burettes of 30 to 50 c.c. capacity, graduated in ⅕ or 1/10 c.c. Instead of a clip there may be used a little piece of glass rod rather more than ⅓ of an inch long inserted in the india rubber tube, and not fitting it too tightly; this stops the passage unless when the tube is drawn to one side with the finger and thumb, a small canal being thus formed, through which the fluid escapes.



a

Cross section of the india rubber tube with the glass rod contained in it.



b

Cross section showing the channel at the side between the rod and the tube formed by the stretching of the latter by the pressure of the finger and thumb.

In using these burettes they should be kept scrupulously clean, particularly the india rubber connections; and before beginning to use them fill completely with the standard solution or fluid, and let some of it escape by the india rubber until the column of liquid stands at 0°. In reading the graduations care must be taken that the tube is vertically placed, and the eye on the same level as the liquid in the tube; the lowest point also of the meniscus is to be selected, and the finding of this can often be facilitated by placing a small card, half of which is white and half black, behind the tube, the upper margin of the black half about on a level with the surface of the liquid.

Measuring Flasks, etc.—One litre flask and one ½-litre flask; one graduated cylindrical glass measure of about 500 c.c. A glass-stoppered test-mixer, graduated, and capable of holding about 2 litres, is useful in the preparation of volumetric solutions.

CHAPTER II.

METHODS AND PROCESSES.

Dialysis.—This term is applied to the separation of diffusible from non-diffusible bodies. Certain substances possess the property of passing readily through animal membranes or vegetable parchment, while others are devoid of it. Thus, if we place some salts in solution in a vessel with a parchment bottom, and immerse the vessel in water, the salts will penetrate the parchment until the densities of the two fluids are alike.

The diffusibility of substances varies greatly, some possessing the property much more than others. Thus, of the four bodies hydrochloric acid, potassic chloride, sodic chloride, and magnesic sulphate the diffusibility is greatest with the first and least with the last.

As a rule diffusion is more rapid with crystalline bodies, while it is slow with non-crystalline bodies like gelatin; and accordingly bodies that pass thus readily through or penetrate membranes or gelatinous masses are called *crystalloids*, while those not possessing the property are named *colloids* (GRAHAM). But it must be remembered that all bodies that crystallize (such as hæmoglobin) do not dialyse, nor are all non-crystalline bodies indiffusible; the non-crystalline peptones, for example, diffuse readily. By this process of dialysis colloidal substances like mucus, albumen, gelatin, gum, etc., can be separated from crystalloids like salts and sugar.

Diffusion is favored by agitation, by an elevated temperature, and by a large surface; and the greater the difference in density between the fluids on each side of the membrane the greater will be the rapidity of the diffusion.

The process will therefore be quickened by changing the external fluid frequently and concentrating that contained in the dialyser. The term *osmose* is applied to this passage of fluids through a membrane, this being simultaneously saturated by both liquids, and, according as the passage is inwards or outwards, the process is named *endosmose* or *exosmose* respectively. The attraction or affinity of the two liquids for each other, and the difference in the attraction the diaphragm exercises on each are the chief factors concerned. The size of the molecules of the substances on each side of the membrane, and of the interstices of the membrane itself, are also of importance. Thus hæmoglobin, although a crystalloid, and albumen, etc., on account of the large size of their molecules, cannot pass through or dialyse. Generally, two currents traverse the membrane in opposite directions, one of which, however, exceeds the other in intensity; but in some cases, as where concentrated colloidal solutions are on one side of the diaphragm and water on the other, the water alone traverses the membrane.

A *dialyser is readily made* by tying a piece of soft, moist bladder or parchment paper over the lower mouth of a glass vessel of conical or bell shape and open above. Care should be taken to tie the membrane on *very tightly*, and the membrane should present no fissures: accordingly, after the tying has been completed, pour water into the dialyser thus made, and note if any traces of moisture appear on the lower side of the membrane, indicating solutions of continuity; this may be noted directly by the eye, or by placing the dialyser on a sheet of blotting-paper. If so, brush some white of egg over these spots, and plunge the membrane into hot water to coagulate the albumen; or, if necessary, stick a piece of fresh parchment over these points by means of the white of egg, the latter being coagulated by passing a hot iron over the patch. The dialyser thus constructed is then placed upon a tripod in a larger vessel filled with water, or it is suspended in it by means of a thread.

Another convenient form consists of a double hoop of wood or gutta percha, the inner hoop being slightly conical and about two inches deep, and the outer about an inch deep, the membrane being fixed between them. This form is used when the liquid to be diffused amounts to eight or ten ounces; and it is allowed to float on water in a larger vessel.

Small Dialysers can readily be made from wide test tubes, the parchment being tied over the mouth and the closed end cut off.

In dialysing, the layer of liquid inside the dialyser should not be much deeper than half or three-quarters of an inch, and it is to be gently agitated from time to time; and the fluid outside ought to be at least four or five times greater in amount.

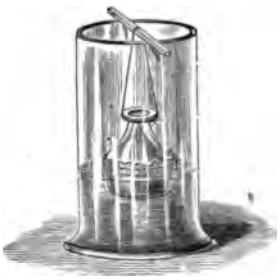


FIG. 3.—DIALYSER.

The inner vessel is closed below with parchment, which is held in its place by a closely fitting double elastic ring.

Decantation.—This is one of the methods employed in *washing a precipitate* that is heavy and subsides readily. The precipitate is vigorously shaken up with successive quantities of water, which is poured off when the precipitate has settled down; and it is advisable to let it run along a wet glass rod held in contact with the margin of the containing beaker. At this point a little lard should be smeared on the outer surface, to prevent the fluid trickling down the outside of the beaker.

If the washing is done on a large scale it is better to make use of a *siphon*. A *pipette* may be employed to suck off the supernatant liquid when it is present in small amount, and sometimes if the layer is very thin it may be removed by the careful introduction of a fold of filter paper.

Siphons and pipettes are also useful in separating two layers of different liquids one from the other.

Desiccation.—By this process the hygroscopic water that adheres so closely to different substances, particularly those of animal origin, is removed. As a great many organic substances begin to decompose at temperatures above 120° to 130° C., it is therefore necessary during the process of desiccation to maintain the temperature between 100° and 120°, and this should be kept constant as far as possible. Many substances bear a temperature of 130° to 140° C. without decomposition, but a *temperature of* 110° *is the most generally useful.*

A square or cylindrical strong copper box that can be readily opened, and which is provided with a perforated shelf whereon to place the dish containing the preparation to be dried, and with an opening in its cover in which a thermometer is fixed, is most frequently used for desiccation purposes. Care must be taken that neither the thermometer nor the drying dish comes in direct contact with the floor or wall of the drying chamber.

A washed precipitate still lying in its funnel, if intended to be dried, may first be placed in a small wire tripod standing upon a sheet of wire gauze or netting that is supported at a convenient height over a flame by another larger wire tripod. When nearly dry transfer the filter with its contents to a water bath; if a higher temperature is required to complete the desiccation recourse may be had to the process that follows.

A good plan for *completing the drying of precipitates* on filters, when they have to be afterwards weighed, is to place the folded filter with its contained precipitate between two watch glasses not hermetically closed, to transfer the latter, after having been fixed with metal clips, to the interior of the desiccating chamber for a quarter to half an hour, when they are to be clipped as tightly as possible—the watch glasses should have ground edges to admit of this—and then to leave them under cover to cool slowly over a dish of sulphuric acid, as described in the following paragraph.

Drying over Sulphuric Acid.—Hygroscopic powders, on account of the rapidity with which they absorb moisture from the air, must, after having been ignited, be allowed to cool under a bell jar, a dish containing sulphuric acid being present. The air in the bell jar is thus maintained in a dry state.

A dry chamber may also readily be formed by means of a large beaker with ground edges, that are to be smeared with lard, and a smooth plate of glass to be laid thereon. The acid is poured into the bottom of the beaker, and the hygroscopic powder placed between two watch glasses loosely secured by a clip; the watch glasses are supported on a little tripod made of three small glass tubes fixed together with lead wire. By placing the beaker with its contents, but without its cover, under the receiver of an air pump, and then exhausting, a powder may be dried without the aid of heat; but the desiccation requires several days.

To Dry Flasks, Tubing, etc.—After the *flask* has drained completely, warm it carefully and suck the air from its interior from time to time with a long glass tube dipping down into it.

Narrow glass tubing may be dried by drawing or pushing a piece of dry filter paper or cotton through it; but with long and very fine tubes recourse must be had to heating some length of them over a flame and subsequently drawing air through with the mouth or otherwise. Small tubes, such as reduction tubes and the like, are readily dried by placing them upon a heated metal plate or in a hot sand bath.

Distillation.—The boiling point—that is, the temperature at which different bodies pass off rapidly in the form of vapor—varies greatly, some being much more volatile than others. Advantage is taken of this in the process of distillation to separate these bodies.

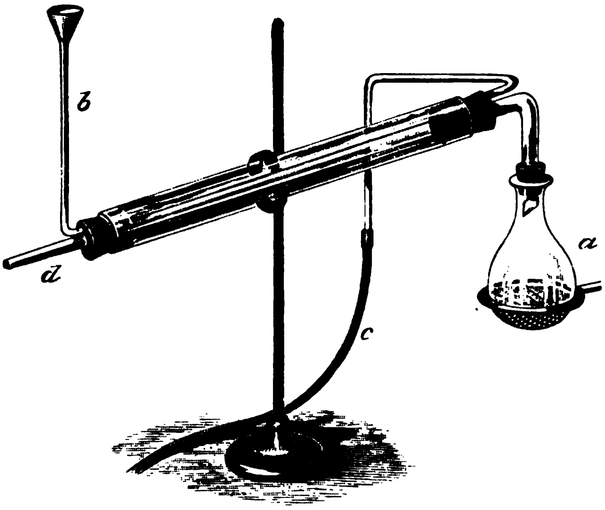


FIG. 4.—SIMPLE DISTILLATION APPARATUS.

The construction is very simple, the condenser consisting of a wide glass tube through which the narrow glass tube from the flask *a* passes. A constant current of cold water is obtained by allowing water to flow from a tap into *b*; it escapes by *c*. The condenser is fitted to *d*. A small glass flask will serve the purpose.

The parts of any distillation apparatus consist essentially of a boiler and of a condenser. A simple form is Liebig's, in which the long neck of a glass retort is inserted into the inner tube of the condenser, that is made of a tapering glass cylinder fixed by perforated corks in the centre of a wider metal pipe. Between these two tubes cold water is made to circulate, the water entering by a long tube near the lower end, and as it is heated rising and flowing out by a small tube near the upper end. By connecting both these tubes, one with a tap and the other with a sink, by means of india rubber tubing, the current is rendered constant. The narrow end of the condenser dips into the flask or receiver into which the condensed liquid drops. Where the neck of the retort is fitted into the condensing tube the connection should be made air-tight by wrapping a ribbon of stretched india rubber round this part of the neck before inserting it.

A thermometer is fixed into the retort by passing it through the cork at its summit, and it should nearly touch the bottom. The heat is gradually applied by a rose or ring burner, or, failing these, by an ordinary Bunsen lamp.

Distillation on a small scale can readily be performed by using a plain retort, surrounding its long neck with some folds of blotting-paper, and keeping this wet by water dropping upon it from a bottle placed at a higher level. Failing a retort, the purpose will also be effected by using a Florence flask with a long bent tube fitting into the cork closing it, and dipping loosely through a perforated cork into another similar flask lying in a basin of cold water.

Evaporation.—The usual temperature employed is 100°,[1] which is easily obtained with the water bath; but when the evaporation is to be done at a lower temperature an air or sand bath can be employed.

To prevent loss of fluid one of these plans can be adopted: (1) Place a small funnel in the mouth of the flask; (2) fix into the cork closing the flask a glass tube, 2 to 4 feet long; this tube may be drawn out to a capillary opening at its upper extremity, if necessary; (3) connect the flask with the condenser of a Liebig's apparatus.

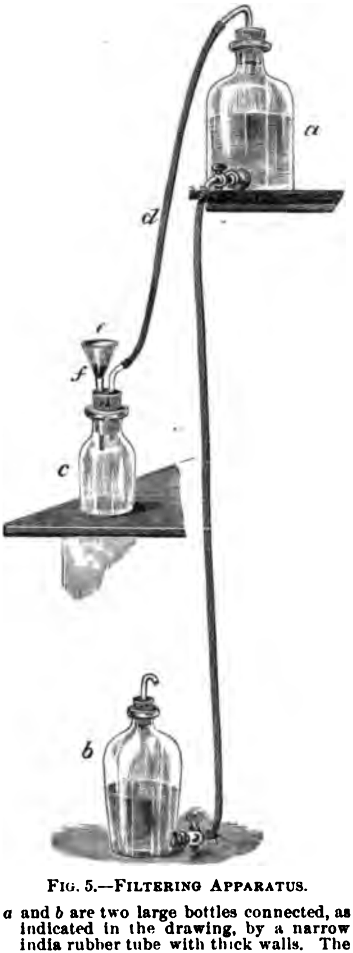


FIG. 5.—FILTERING APPARATUS.

a and *b* are two large bottles connected, as indicated in the drawing, by a narrow india rubber tube with thick walls. The upper bottle should be placed as high as possible. *c* is a bottle into which the filtrate is to pass. The interior of this is in connection with *a* by a thick-walled tube *d*. Into the stopper of *c* the funnel *e* is fixed, and at its apex lies the small platinum funnel *f*, which supports the apex of the filter when the interior of *c* is partially exhausted by the discharge of the water in *a* into *b*.

Ethereal or *alcoholic solutions* are to be evaporated over a water bath, and not over a naked flame. In evaporating *albuminous solutions* avoid charring, and stir frequently with a glass rod during the operation.

In heating beakers care should be taken not to apply the naked flame, but let the beaker be placed over the flame on a wire gauze, or on a flat iron plate supported on a tripod. A sand bath may also be employed.

The maintenance of a constant temperature is best effected by a gas regulator (Bunsen's or Page's). Roughly it may be accomplished by carefully regulating, with the help of a thermometer, the size of the flame of a burner applied to a sand bath, or to a small metal chamber surrounded by a double wall in which water is contained.

Filtration.—The filter should always be smaller than the funnel in which it is inserted, and generally it should be moistened with water before being used. Ribbed filters are employed for quick filtrations, when the filtrate alone is wanted; or the filter may be allowed to rest upon three or four glass rods hooked on to the upper edge of the funnel.

Double funnels are sometimes required, especially when it is desired to keep the filtering fluid hot during its passage through. A double funnel may easily be fitted up by placing a glass funnel inside a larger tin funnel, so that a space may intervene between them, the tube of the glass funnel passing through a perforated cork fixed in the lower extremity of the tin funnel. Warm water is allowed to flow into the space between the two from above, and to escape through a small tube below.

---

[1] When not otherwise indicated, the temperatures will be given in the centigrade scale.

With voluminous, dense, or mucilaginous deposits, first pass through linen or fine muslin, and if necessary through an additional coating of flannel.

Filtration may be greatly accelerated by reducing the pressure inside the vessel into which the liquid is flowing. This can be effected as follows: Two large glass jars are connected as in the diagram, and the interior of the vessel in which the filter is fixed is brought into connection with the upper glass jar. The funnel, which must be perfectly smooth in its interior, passes tightly through the cork, and is accurately fitted with a little perforated cone of thin platinum, in which the apex of the filter rests. The upper jar is filled with water, and when this is allowed to discharge itself into the lower jar a partial vacuum is caused on the lower level of the filter.

Incineration.—By this operation the fixed salts of an organic or inorganic compound may be obtained. It can be performed in a small porcelain or platinum crucible supported in an inclined position on a pipe-clay or platinum-wire triangle; but a platinum crucible is not to be used if the substance to be ignited evolves chlorine, bromine, or iodine, or contains phosphorus or phosphates, or if alkaline nitrates, easily oxidized metallic oxides, or organic salts of the heavy metals are present; in such cases the porcelain crucible is to be preferred.

It is necessary, before igniting, to dry the precipitate thoroughly, and then to detach it from the filter as completely as possible over a sheet of smooth paper; the collected precipitate, transferred to the crucible, is then to be cautiously ignited to a dull red heat over a Bunsen lamp, the crucible being covered for the first few minutes of the calcination and then uncovered. Now cut the dry filter into small pieces and ignite them upon the cover of the crucible, add the ash to the crucible, and having again applied the cover, subject the whole to a higher temperature if necessary.

When the crucible is to be weighed it should first be allowed to cool over sulphuric acid in a bell jar.

It should be remembered that a continued red heat causes some of the elements of the ash, such as chlorine, etc., to be volatilized, and sulphuric acid to be decomposed in presence of the organic carbon, part of the sulphur formed escaping as sulphurous acid. The grouping also of the elements of the ash is different to that of the salts in the organic body. To obtain more accurate results the dried substance should first merely be carbonized, and the soluble salts (alkaline chlorides, phosphates, and sulphates, etc.) then removed by washing; this done, the residue is again dried, and ignited till a white ash is obtained.

Preparation of Normal Solutions.—The directions given for the preparation of solutions on the gram system can also be applied to their preparation according to the weight in grains. If grain weights are used instead of grams, then move the decimal point one place to the right: thus instead, say, of 6·53 grams, 65·3 grains; and for each c.c. use 10 grains.

These normal solutions as a general rule are of such a strength that 1 litre at 15° contains the hydrogen equivalent of the reagent in grams. A normal solution of hydrochloric acid, for example, must contain ($H=1+Cl=35{\cdot}5=36{\cdot}5$) 36·5 grams of the acid in a litre of water. But in the case of a bivalent substance the equivalent is half the atomic or molecular weight: thus a normal solution of the dibasic oxalic acid ($C_2H_2O_4+2H_2O=126$) contains 63 instead of 126 grams dissolved in the litre of water.

But solutions are also prepared of decinormal or centinormal strength; and sometimes, for the sake of convenience, solutions are prepared more or less empirically, as according to the amount of oxygen they liberate, etc.

Indicators of the Termination of the Reaction in Volumetric Analysis.—These vary considerably, in some cases the termination being shown by a change of color, as in alkalimetry, where the standard acid is added to the alkaline solution until the litmus present in the latter alters in color from blue to red; or in Fehling's process for the determination of sugar, where the final reaction is known by the disappearance of the blue color. In alkalimetry the indicator is added at the beginning of the experiment; the same is done in many other estimations, but in some the end of the process can only be determined by an indicator separate from the solution, as in the estimation of urea by mercuric nitrate, where the latter is added to the urea solution until a drop of the mixture, when brought in contact with a drop of sodic carbonate solution on a porcelain plate, produces a yellow color.

Specific Gravity.—The specific gravity of such a fluid as urine is generally obtained by the urinometer. But when it is required with greater accuracy we employ a small-density flask of known weight (pycnometer) fitted with a stopper through which a capillary canal passes, and containing, when filled, a known quantity of water (about 25 to 30 grams) at 15·5°. This is to be rinsed out, and then filled with the liquid whose density is required. After weighing the specific gravity is obtained by the formula: specific gravity$=\frac{W\times 1000}{W'}$; W'=weight of water and W=weight of liquid.

CHAPTER III.

NUTRITION.

THE constituent parts of the organism are gaseous, liquid, and solid. Of the gases oxygen, nitrogen, and carbonic anhydride are the chief, and these are generally in a state of solution in the liquids, the largest proportion of which consists of water holding in solution different acids, salts, and organic bodies. The solids have generally a complex constitution, and form the framework of the organism. Nutrition has for its function the maintenance of these component principles, which, owing to their vitality and to the changes to which they are subjected, require constant renewal. The body may, in a sense, be regarded as a complicated machine in which a certain amount of work is done involving so much waste—in which, in short, the potential energy supplied by the food is converted into the actual energy of heat and mechanical labor; although we should not be justified in comparing the body to a furnace for the direct combustion of the food, for there is much reason to believe that, instead of this direct conversion and elimination of energy, the food may first be mainly changed into tissue, and that then it undergoes the changes which end in its becoming waste product. In effecting this conversion the animal economy acts as a more perfect machine than the best steam engine, for HELMHOLTZ has shown that while in the steam engine only one-tenth of the energy of the fuel is utilized as mechanical work, fully one-fifth of the energy of the food is realized by the human machine.

In addition to the waste dependent on the work done there is also the waste due to the wear and tear of the organism itself. The products of all this waste are removed by the function of *elimination* in the urine, sweat, and fæces, etc.; and the consequent losses thus incurred are restored by the instrumentality of the function of *digestion*, in which new materials are introduced from without and fitted by *assimilation* to replace the particles that have been removed; and, to burn the fuel thus introduced and render its energy convertible, constant supplies of oxygen are obtained by the lungs in *respiration*. There is therefore in the living body, at every moment of its existence, an arrival of new and a departure of old molecules, and consequently an uninterrupted succession of chemical reactions. For all these processes to go on a certain temperature must be maintained; this is derived from the sum of the oxidations occurring, and the balance is so well regulated that a uniform temperature is kept constant.

According as the body takes up more or less than, or the same amount as, it loses, so will the body weight increase or diminish proportionally, or maintain itself unchanged. In this last case, with a man of average weight and activity, about 6,000 grains of dry solids and 30,000 to 40,000 grains of water are required to be taken up by absorption (RANKE), and about 10,000 grains of oxygen by respiration; of which about 800 grains of the solids are eliminated by the intestines, and the remaining 5,200 by the other excretions, the oxygen also being discharged in combination with them, after having burnt them up in the body, and thus converted their latent or potential into kinetic energy. We may state loosely that in this way a daily loss occurs nearly equal to one-twentieth the body weight. By the term *potential* energy, it may be explained, is meant the passive energy of position—that is, energy capable of performing work when called upon, such, for example, as resides in a bent cross-bow or in water confined at a high level. By *actual or kinetic* energy, on the other hand, is understood energy doing work, as when the bent bow is suddenly unbent and causes an arrow to fly through the air; or when the water escapes, and in doing so causes a mill-wheel to revolve, by which machinery is set in motion.

In early life *the nutritive powers of the tissues* are more active than the oxidizing processes, and so growth and development occur; in adult life they are nearly balanced, and more or less of an equilibrium is maintained; but in old age the processes of nutrition are defective, and the wasting processes are in excess, and accordingly a failure occurs in tissue regeneration and in the maintenance of the animal temperature. The nutritive processes are also diminished during sleep, the carbonic acid eliminated during the night being one-fourth less than during the day (SCHARLING), the production of urea likewise being lessened; the absorption of oxygen, however, still continues, and the result is that an accumulation of oxygen in the organism occurs during sleep.

A constant and unintermittent supply of oxygen is an absolute necessity, and it may therefore be regarded as our most important food. Almost every vital act in the body may be said to be accomplished by oxidation and a corresponding consumption of oxygen. Indeed, between the food and the absorbed oxygen an interplay of changes is essential to the maintenance of the vital functions, whether these consist in the production of heat, in muscular contraction, in mental activity, or in assimilation. By this oxidation the energy therefore necessary for the manifestation and continuance of these bodily functions is obtained by the burning up of the constituents of the food, the ultimate products of the oxidation, which is effected by a series of successive steps, being urea, carbonic acid, and water. For example, the complete combustion of 10 grains of dry flesh raises 13·12 lbs. of water 1° F., and is equal to lifting 10,128 lbs. one foot high; while that of 10 grains of sugar raises 8·61 lbs. of water 1° F., and is equal to lifting 6,647 lbs. one foot high (FRANKLAND). Or an ounce of lean meat entirely burnt in the body produces heat sufficient to raise 70 lbs. of water 1° F., or a gallon of water about 9° F.; while an ounce of fresh butter, if completely consumed in the body, would produce ten times that amount of heat (E. SMITH).

HEIDENHAIN calculates that four-fifths of the total energy of the body takes on the form of heat. In the active muscles, and in glands in a state of activity, especially the liver, a considerable elevation of temperature can be observed, pointing to these parts as generators of heat.

The tissues are bathed in the lymph, which is spread out in all their interstices throughout the organism, and is so abundant as to have been estimated at one-third the body weight by KRAUSE, or about one-fourth by LUDWIG. Without ceasing, exchanges occur between this fluid and the tissues bathed in it, and the interchanges consist, so far as the tissues are concerned, in certain additions to and subtractions from the lymph; these then constitute *nutrition* properly so called. Osmotic transferrences continually occur between the lymph and the blood, and the blood is renewed by the products of assimilation. Betwixt the fluid directly bathing and nourishing the tissues and the food prepared for absorption by the digestive processes the blood acts as a "go-between" or intermediary, being replenished thereby, while it is freed from the effete additions that have been made to it by means of the lungs and the organs of excretion. Taking muscle as exemplifying some of these nutritive changes, we find, so far as the tissue itself is concerned, that its soluble albumen diminishes as it contracts, sarcolactic acid, inosit, kreatin, and carbonic anhydride making their appearance. The elimination of water, chlorides, and phosphates is also increased with the muscular activity, and the amount of oxygen absorbed likewise proportionally augmented. As to the greatly increased elimination of urea that LIEBIG supposed also to take place, the weight of evidence is opposed to the hypothesis. A slight but temporary increase probably occurs, but it bears no relation to the amount of work done (PARKES). Theoretically, too, the amount of albumen corresponding to the slightly increased quantity of urea excreted is incapable of furnishing even a small proportion of the energy expended, or, even when totally oxidized, of giving off the excess of carbonic acid disengaged in the process. Rather it appears that a notable proportion of the heat transformed into muscular energy during muscular activity is due to the combustion of non-azotized rather than of azotized materials.

Nutrition in nerve appears to follow the same laws as in muscle, and probably as the result of its activity we have an increased absorption of oxygen and an increased excretion of cholesterin, urea, carbonic acid, and phosphates. Intellectual work is always attended with an increased flow of blood to the nerve centre, and with a rise of temperature of the nerve substance. Nerve also, which is neutral in a state of repose, becomes acid when strongly excited, the acidity of the urine increasing with prolonged mental exertion (FUNKE). According to WOOD the earthy phosphates excreted are diminished by intellectual labor, while the alkaline phosphates undergo little or no increase.

CHAPTER IV.

FOODS.

FOODS.—A body capable of replacing any of the body waste, or of imparting heat to the organism by its oxidation—in short, any substance supplying material that renews waste or maintains any vital process—may be regarded as a food. VOIT further regards in the light of a food any substance that prevents the removal from the body of any of its necessary constituents. Grape sugar, when burnt up, forms carbonic acid and water, $C_6H_{12}O_6+6O_2=6CO_2+6H_2O$, eliminating much heat in the process, and accordingly is a source of heat and energy to the system. The sugar, which was formed in a vegetable organism at the expense of the sun's light and heat, has this energy stored up in it, ready to be converted from the potential to the kinetic condition under favorable circumstances.

Albumens and fats act in the same way, and are stores of so much force that may show itself in heat, motion, or otherwise, or in a combination of them. All these sources of energy come directly or indirectly from the vegetable kingdom, and are therefore primarily derived from the sun's energy, plants having the power of fixing the solar force. In animals, on the contrary, potential is converted into kinetic energy, but they also possess a certain amount of constructive energy, and, working upon organic matter already formed, they can build up higher combinations. A good example of this we see in the hæmoglobin of blood.

Food, as we have seen, maintains by its oxidation the animal heat, and restores the waste resulting from animal activity. The body consists of proteids, fats, carbohydrates, water, and salts, and to maintain it these bodies must be supplied in the food, although it must not be supposed that there is a direct conversion of the food elements into the corresponding tissue elements. Thus the nitrogenous food does not supply alone the nitrogenous tissues, for we shall see that even in the alimentary canal part of it is broken down, and no doubt also, after its absorption, still further altered, so as to be a source of the fat of the economy. In fact, as a general rule the elements of the various food stuffs undergo more or less of a rearrangement before they take their place as bodily constituents.

For a healthy man the food of the twenty-four hours should contain some 4,000 to 5,000 grains of carbon, and 250 to 300 grains of nitrogen; the food supplied should therefore possess these elements in their proper proportions, otherwise it will not be economical in any sense of the word.

In the forms of albumen, fibrin, casein, and legumin, which are all readily assimilable, the required nitrogen is furnished to the system. The extractive matters also present so largely in flesh meat and the like, supply more of the same, but whether they form a distinct source of energy is still doubtful. The salts of muscle, however, aid the assimilation of proteids; and the same purpose is likewise effected, in some degree, by the ingestion of starchy and fatty foods. Some of the carbon is supplied by these albuminous bodies, but the great mass by the starches, sugars, and fats. These carbohydrates, when directly absorbed, as well as those (such as inosit and glycogen) proceeding from the decomposition of albuminoid bodies, seem to be the source of rapid heat production in the system.

The *dynamic value of a food* depends on its richness in easily assimilable proteids, and its *calorific value* on the quantity of heat it produces when burnt in the organism. But the *digestibility* of a food must also be taken into consideration, as this is more a measure of its nutritive value than its elementary composition. Great differences exist in the absorption of different foods: thus rye bread, potatoes, and green vegetables produce large quantities of fresh and dry excrement; while white bread, fresh meat, and eggs are absorbed to a greater extent, and are therefore more valuable. Fat of butter also appears easier of digestion than bacon fat; and carbohydrates are easily assimilated when contained in white bread, rice, and macaroni, but with more difficulty from potatoes, rye bread, and turnips; further, nitrogen is most easily absorbed from meat, eggs, and animal substances generally, but with more difficulty from rye bread and vegetables (RUBNER).

Where the final consumption of the food particles occurs is still to be decided, but it is probable that before the final decomposition products—water, carbonic acid, and urea, ammonia, or some such body—are reached, a series of retrograde and intermediate processes have occurred in the living cells of the tissues themselves, and in the fluids immediately bathing them; and it is possible that some of these changes normally take place in such great central vascular organs as the liver and spleen.

In the normal condition an equilibrium is maintained between the ingesta and the egesta. The following table, giving the results of a series of three days' experiments made on a dog, shows this distinctly (PETTENKOFER and VOIT):

A. *Food:* flesh, 1,500 grams; oxygen absorbed, 477·2 grams; total, 1977·2 grams.

The flesh.		C.	H.	N.	O.	Mineral salts.
Dry solids . . .	361·5	187·8	25·95	51·0	77·25	19·5
Water	1138·5	0	126·5	0	1012·0	0
Oxygen absorbed .	—	0	0	0	477·2	0
Total . . .	1500	187·8	152·45	51·0	1566·45	19·5

B. *Excretions:* total, 2011·8 grams.

			C.	H.	N.	O.	Mineral salts.
Dry solids and gases	704·7	Urea	21·6	7·2	50·4	28·8	0
		Organic salts of urine	9·6	2·5	0	15·9	16·3
		Dry fæces	4·9	0·7	0·7	1·5	3·4
		Carbonic anhydride by lungs and skin . .	146·7	0	0	391·5	0
		Marsh gas by lungs and skin	1·2	0·4	0	0	0
		Hydrogen	0	1·4	0	0	0
Water excreted	1307·1	Water of urine	0	102·5	0	820·3	0
		Water of fæces . . .	0	3·2	0	26·3	0
		Water by lungs and skin	0	39·4	0	315·4	0
	2011·8		184·0	157·3	51·1	1599·7	19·7

All the nitrogen leaving the body is calculated as urea, which gives a slight excess. It is to be remarked also that while the dog absorbed only 1138·5 grams of water, he excreted 1307·1 grams, from which it follows that the 168·6 grams in excess have been formed at the expense of the tissues or organs. Of the 477·2 grams of free oxygen absorbed, 391·5 are excreted in combination with carbon as free carbonic anhydride, and 149·9 grams in combination with hydrogen as water, or in the proportion of 3 to 1, a proportion which in man is about as 7 to 1. Of every 100 degrees of heat produced, therefore, in the living organism, 81·5 are due to the combustion of carbon and 18·5 to the combustion of the hydrogen of the food ingested.

Taking all these facts into consideration, the *best food for repairing the losses of the organism* would be one consisting of—

	Grains.
Dry proteids	1,913
Dry starches	6,172
Fats	1,142
Total	9,227

requiring about 11,000 grains of oxygen for their combustion, giving for these bodies respectively nearly the relative proportions of 1:3·20:0·6, or 1 of proteids to 3·8 of the combined starches and fats; proportions closely corresponding to those given by Moleschott, who established the relation of the proteids to the two other combined foods, as 1:3·75. Liebig gave it as 1:3, and that of the fats to the starches as 1:5·4. These proportions would be obtained in a daily food made up of white bread, 1·8 lb., lean meat, 0·53 lb., and fat, 0·13 lb.

Proportion of the Chief Tissues forming the Human Body.
(BISCHOFF.)

	Man (æt. 33).	New-born male child.	Weight in adult as compared with that of the infant taken as 1.
	Per cent.	Per cent.	
Muscles	41·8	22·9	28
Fat	18·2 with skin.	20·0	—
Skeleton	15·9	17·7	26
Abdominal viscera	7·2	11·5	15
Skin	6·9	11·3	12
Brain	1·9	15·8	37
Thoracic viscera	1·7	3·0	17

The muscles thus form nearly half of the body, and they contain quarter its total blood; and of the abdominal viscera the most important is the liver, which also contains about a fourth of the whole blood.

The chemical composition of the different tissues will be taken up subsequently. Reference will be made here only to the water and the salts entering into their constitution.

Water forms about 70 per cent. of the adult and 88 per cent. of the embryo, and is the medium in which the chemical changes of the organism occur. In the accompanying table the average proportion of water in several of the tissues is given:—

	Per cent.		Per cent.
Lymph	93–96	Brain	75
Chyle	90–95	Cartilage	67–73
Blood	78	Bones	13
Kidneys	82	Teeth	10
Nerves	78	Enamel	0·2
Muscles	76		

Salts.—The mineral salts form 3 to 6 per cent. of the adult's body, and about 1 per cent. of that of the fœtus. They are obtained as ash when the tissues are calcined, but part of them result from the oxidation of the sulphur and phosphorus of some of the organic constituents. The heat also decomposes and volatilizes a few of the components, such as certain chlorides and carbonates. It must, therefore, be remembered that the analysis of the ash does not represent the true composition of the salts as they existed in the living tissue. Alkaline chlorides and phosphates, earthy phosphates, with some carbonates and sulphates form the chief of these salts, of which *sodic chloride* is the most important, its presence exciting assimilative changes and assisting in the secretion of many of the juices, particularly the gastric; and so necessary is it to the organism that when it is supplied in insufficient quantity it is retained by the tissues and not excreted. When deprived of it animals lose weight, spirits and activity. The *potash salts* are also indispensable, acting as exciters of the nervous system and increasing the cardiac pulsations.

A great daily loss occurs in the salts, which, of course, must be restored in the diet. By the urine of a healthy man of average weight, for example, there is a daily discharge of about 180 to 250 grains of chloride of sodium and about 120 to 130 grains of other salts, and by the fæces about 130 to 140 grains of different salts. These salts are principally phosphates of potash and phosphates and carbonates of lime, etc. Accordingly the food should contain at least 250 grains of sodic chloride and about half that amount of other salts, especially those of potash, to make good this daily loss.

The distribution of these salts in some of the organs and fluids of the body can be seen in the adjoining table (after Gautier):—

Ash.	Brain.	Muscle.	Milk.	Blood.	Yolk of egg.
Potassium	32·4	34·4	21·4	11·2	8·9
Sodium	10·7	2·4	—	6·3	5·12
Magnesium	1·23	1·45	0·87	1·26	2·07
Lime	0·72	1·99	18·8	1·85	12·1
Sodic chloride	4·7	10·6	10·7	36·3	—
Potassic chloride . .	—	—	26·3	26·5	—
Phosphoric acid . .	48·1	48·1	19·1	8·8	78·9
Sulphuric acid	0·75	—	2·6	7·11	—
Silica	0·42	0·81	—	—	0·5

Saline matters are evidently associated with the different formative processes occurring in the body, and we find no indiscriminate diffusion, but a regular and special distribution of them in the different organs and tissues of the organism. It is easy to see, then, that mineral salts require to be supplied for the nutrition and growth of the different parts of the system, and also for the formation of the secretions. So important indeed are the salts of the food that animals dieted with food from which all inorganic salts have been removed rapidly die off (Forster), due partly, in Bunge's opinion, to the formation of free sulphuric acid from the albuminoid sulphur, and the consequent abstraction of basic constituents from the intestines.

The combinations therefore required are salts of lime, magnesia, potash, soda and iron, with chlorine, phosphoric and sulphuric acids, the lime and phosphoric acid appearing to be specially important. All these combinations are present in the meat, bread and fresh vegetables ingested. As examples we shall cite here the composition of the ash of wheat and milk in the 100 parts.

	Ash of wheat.	Ash of cow's milk.
Phosphoric acid (P_2O_5)	43·5	28·40
Potash	32·4	23·46
Magnesia	13·9	2·2
Lime	3·5	17·34
Silica	3.05	—
Soda	2·3	6·96
Ferric oxide	1·0	—
Sulphuric acid	0·35	—
Potassic chloride	—	14·18
Sodic "	—	4·74

Potash salts are abundant in the potato, constituting more than 50 per cent. of the ash, which is, however, not very abundant, varying from 0·8 to 1·3 per cent. of the fresh potato.

The alkaline citrates, tartrates, and malates of the vegetables eaten are burnt in the organism to the state of carbonates.

Mixed Diet.—Different experimenters have proved that a normal food must not consist of one aliment exclusively (CHOSSAT, RANKE), whether nitrogenous, starchy, or fatty; further, as no one food contains the different essential principles in the necessary proportions, a mixed diet must be employed, and the nature of this diet must vary with the manner of living, with the climate, and with the seasons. The diet must also be in sufficient quantity, and without any excess in the animal or vegetable components.

The necessary nitrogen and carbon will accordingly be best, and so far as the organism is concerned, most economically obtained from a mixed dietary. Upon it, indeed, man appears to attain to his finest development of physique and highest vigor of intellect; this mixed diet at the same time being most conformable to the character of his teeth and digestive apparatus. A diet, however, from which meat is largely excluded may often, it may be observed, be used with advantage, but under most circumstances the most suitable admixture contains one-fourth or rather more of animal food. Thus 2 lbs. of bread and ¾ lb. of beef will supply the necessary amounts of carbon and nitrogen, which would require over 6 lbs. of meat and more than 4 lbs. of bread if either is taken singly; these amounts, moreover, giving a large surplus of carbon in the case of the bread and of nitrogen in the case of the meat.

Classification of Foods.—DUMAS and LIEBIG divided foods into *assimilable* or *plastic* and *combustible* or *respiratory;* but, as all foods are in reality plastic, the division is an inaccurate one. More correctly foods may be classified, according to their composition, into—

Organic	Nitrogenous	Albumens, etc.
	Non-nitrogenous	Fats. Carbohydrates, together with the alcohols and vegetable acids.
Inorganic	Water. Salts.	

RANKE maintained himself in good health, neither losing nor gaining weight, on a diet of this kind:—

	Grams.	Grains.
Proteids	100	1,540
Fat	100	1,540
Amyloids	210	3,700
Salts	25	380
Water	2,600	40,120

Diet for a Working Man of Average Height and Weight (MOLESCHOTT).

	Grams.	Ounces.
Albuminous matter	130	4·58
Fatty "	84	2·96
Carbohydrates	404	14·25
Salts	30	1·06
Total	648	22·85

The preceding 23 ounces of dry solids would correspond to rather more than double that amount of ordinary solid food, with which requires to be associated about 60 to 80 ounces of water.

On a previous page it is stated that 2 lbs. of bread and ¾ lb. of lean meat will supply the necessary carbon and nitrogen required. In the annexed table, which gives a suitable diet for active laborers, we shall compare the two dietaries.

Diet of Active Laborers. (PLAYFAIR.)		Bread, 2 lbs.	Lean meat (uncooked), ¾ lb.	Bread and meat.
	Oz.	Oz.	Oz.	
Nitrogenous matter . . .	5·0- 5·6	2·59	2·32	4·9
Fat	2·4- 2·9	0·51	0·43	0·9
Carbohydrates	17·9-22·2	16·32	—	16·3
Minerals	0·7- 0·9	0·74	0·61	1·3

In these dietaries the nitrogenous matter present forms one-fifth to a little more than a sixth of the total solids.

CHAPTER V.

THE NITROGENOUS FOODS.

NITROGENOUS FOODS.—The chief of these are the *albumens*, albumen by itself forming by far the most important single element, since it contains nutritive material in a condensed and easily assimilated form, its composition being more or less identical with the albumens of blood and the animal tissues. Examples of rich albuminous foods are white of egg, casein, legumin, gluten, and syntonin. Next come the *collagens*, or bodies that yield gelatin, or an analogous substance, on boiling, as ossein and chondrin; then there are such bodies as kreatin, kreatinin, xanthin, and the like, which may be regarded as disintegration products of the proteids, and which are present in meats. In the table a series of different articles of food rich in these albuminous principles are compared.

A. **Animal Albumens.**

Rich Albuminous Foods (*after* RANKE, PAYEN, LETHEBY, *etc.*)

	Lean raw meat.	Fat raw meat.	Roast meat, no dripping lost.	Lean mutton.	Fat mutton.	Veal.	Fat pork.	Dried bacon.	White fish.	Salmon.	Oysters.	Eggs.
Nitrogenous matter	19·3	14·8	27·6	18·3	12·4	16·5	9·8	8·8	18·1	16·1	14·01	14·0
Fat	3·6	29·8	15·45	4·9	31·1	15·8	48·9	73·3	2·9	5·5	1·51	10·5
Salines, etc. . . .	5·1	4·4	2·95	4·8	3·5	4·7	2·3	2·9	1·0	1·4	4·09	1·5
Water	72·00	51·0	54·00	72·0	53·0	63·0	39·0	15·0	78·0	77·0	80·39	74·0

Composition of Beef, Veal, and Pork (MOLESCHOTT).

	Soluble albumen and hæmatin.	Myosin, etc.	Gelatins.	Fats.	Extractives.	Kreatin.	Ash.	Water.
Beef . . .	2·25	15·21	3·21	2·87	1·39	0·07	1·6	73·39
Veal . .	2·27	14·36	5·01	2·56	1·27	—	0·77	73·75
Pork . . .	1·63	15·50	4·08	5·73	1·29	—	1·11	70·66

If the *yolk is compared with the white of an egg* it will be found that of the nitrogenous constituents there are 20·4 per cent. in the white and 16 in the yolk, 30 per cent. of fat in the yolk, 1·6 per cent. salines in the white and 1·3 per cent. in the yolk, and 78 per cent. of water in the white and 52 per cent. in the yolk.

Good new milk contains about 546 grains carbon and 43 grains nitrogen in the imperial pint.

	Water.	Nitrogenous constituents.	Sugar.	Fat.	Salts.
Milk { New	86	5·5	3·8	3·6	0·66
Milk { Skim	88	4·0	3·8	1·8	0·8

The essential constituent of *cheese* is the casein or curd of milk. Cheeses vary very much in their composition, but an average good skim-milk cheese contains: water 44 per cent., nitrogenous constituents 44·8, fat 6·3, and salts 4·9; and a good new-milk cheese: water 36 per cent., nitrogenous constituents 28·4, fat 31·1, and salts 4·5. Cheeses like the former require a longer time for digestion than the latter, which take about 3 to 3½ hours if of medium age. Cheese contains calcic phosphate and oxide of iron, and there is present in dried cheese deprived of fat and prepared from fresh milk 3·5 to 4 per cent. phosphoric anhydride and 4·3 to 4·7 per cent. lime.

Analyses of Cheeses.

Cheese.	Nitrogenous constituents.	Fats.	Salts.	Water.	
Cheshire	36·14	25·48	4·78	30·39	(MALAGUTTI.)
Gruyère	35·10	28·00	4·79	32·05	
Roquefort	32·95	32·31	4·45	26·53	
Cheddar	28·4	31·1	4·5	36·0	(PAYEN.)
Gruyère	31·5	24·0	3·0	40·0	
Camembert	18·9	21·0	4·7	51·9	(PARKES.)

B. The **Vegetable Albumens** are not so rich in carbon as the animal albumens, but are richer in nitrogen; this probably accounts for their less nutritive value and the greater difficulty in their assimilation; they are, however, like eggs and fish, very rich in phosphorus. It may be stated generally that vegetables are more difficult and slower of digestion than most animal foods, but that when combined with the latter in suitable amount the digestion is rendered easier and the assimilation more perfect. Garlic, onions, radish, turnips, etc., excite the digestion, and at the same time stimulate the urinary and generative organs.

Analyses of Vegetable Grains, Seeds, etc.

(PAYEN, LETHEBY, BOUSSINGAULT, ETC.)

	Starch, sugar, and dextrin.	Proteids.	Fats.	Cellulose, etc.	Minerals.	Water.
Wheat	68·9	14·6	1·2	1·7	1·6	14·0
Rye	67·5	9·0	2·0	3·0	1·9	16·6
Oats	61·5	11·9	5·5	4·1	3·0	14·0
Rice	78·30	6·43	0·43	0·5	0·68	14·4
Barley . .	63·6	13·4	2·8	2·6	4·5	13·0
Peas	58·5	25·4	2·0	1·9	2·5	9·7
Beans	48·3	30·8	1·9	3·0	3·5	12.5
Indian corn . .	65·1	11·1	8·1	—	1·7	14.0
Potatoes . . .	21·09	1·6	0·11	1·64	1·56	74.0
Carrots	14·5	1·3	0·20	—	1·0	83.0

The amount of proteids in potatoes is given by E. SCHULTZE as varying between 0·65 and 1·19 per cent., but as 2·34 per cent. by HOLDEFLEISS. The ash of potatoes is very rich in potash salts.

Analysis of Bread and Biscuit.

	Flour bread.	Biscuit.
Carbohydrates	51·0	73·4
Nitrogenous constituents	8·1	15·6
Fats	1·6	1·3
Minerals	2·3	1·7
Water	37·0	8·0

Analyses of Fruits (FRESENIUS).

	Apples (white).	Pears (sweet red).	Green gages.	Cherries (sweet red).	Grapes (white).	Gooseberries (large red)	Strawberries.
Sugar	7·58	7·94	3·4	13·11	13·78	8·06	7·57
Free acid (expressed as oxalic) .	1·04	trace	0·87	0·35	1·02	1·35	1·13
Albuminous substances . . .	0·22	0·24	0·40	0·90	0·83	0·44	0·36
Pectous substances and pectose . .	3·88	5·10	12·52	3·73	1·43	1·26	1·12
Ash	0·44	0·28	0·39	0·60	0·36	0·31	0·48
Insoluble matter .	1·8	3·51	3·89	5·9	2·59	2·99	1·96
Water	85.04	83·01	79·72	75·37	79·99	85·56	87·47

In mixed vegetables it may be stated generally that 1 lb. contains about 420 grains carbon and 14 grains nitrogen. *When potatoes are compared with bread* as to nutritive power, it will be seen that 1 lb. of bread is equal to 2½ lbs. of potato in carbon and to 3½ lbs. in nitrogen. Some recent *analyses of cabbages* show that they are richer in nitrogenous substances than has hitherto been supposed, the total albuminoids ($N \times 6·25$), in the dry matter of the leaves averaging 12 to 28 per cent., and in the stems 11 to 15 per cent. (LEIZOUR and NIVET). Edible *mushrooms*, although difficult of digestion, are rich in proteids, containing as much as 52 per cent. of nitrogenous matter in the dry state. An analysis of PAYEN'S gives the following:—

Nitrogenous matter and traces of sulphur	4·68
Fatty matter	0·39
Cellulose, dextrin, and sugar	3·46
Salts (phosphates and chlorides of the alkalies, lime, and magnesia)	0·46
Water	91·01

Tea cannot be regarded as a nutriment in the sense of supplying material to maintain structure and generate heat; it rather tends to excite vital activity, particularly acting as a respiratory stimulant. But while tea alone affords little nutritive material the addition of sugar and milk converts it into a useful food.

Analysis of Tea (PELIGOT).

	Per cent.		Per cent.
Theine	2·0–3·0	Fat	4·0
Casein	15·0	Vegetable fibre	20·0
Gum	18.0	Minerals	5·0
Tannin	26.25	Water	5·0
Starch	0.75		

Coffee also excites the nervous system, but not to the same degree as tea, whilst it somewhat depresses the respiratory function. It exerts a marked sustaining influence under fatigue and privation, and it appears to diminish the waste of the tissues (LEHMANN), or to render the elements of the body more stable (GASPARIN), thus economizing other nourishment; but both theories are doubtful (ROUX).

Among vegetables we may distinguish—

1. *Those rich in albumen and nitrogen*—cabbage, asparagus, cress, mushrooms, and truffles. These are all very nutritious, the two latter yielding from 3·1 to 7 per cent. nitrogen (SCHLOSSBERGER). The young cabbage contains from 1·5 to 2 per cent. of nitrogenous ingredients (ANDERSON).

2. *Those rich in mucilage and salts*—white beet, lettuce, and endive. They contain much water, mucilage, inulin, and malates, oxalates, etc., especially of potash and lime. Potash salts predominate in sour kraut, Brussels sprouts, and asparagus, and soda in spinach, etc.

3. *Those rich in acids*—sorrel, tomato, rhubarb, asparagus. They are useful as excitants of digestion.

4. *Those containing little or no starch*—lettuce, endive, spinach, asparagus, artichoke, leeks, white onions, and parsnips.

5. *Those rich in sugar*—beet roots, Jerusalem artichokes, carrots. Ripe fruits also contain much sugar.

Among fruits we may also distinguish (GAUTIER)—

1. *Those containing much sugar*—pears, apples, peaches, apricots, prunes, melons, oranges, strawberries, figs, grapes, &c. When ripe they are easy of digestion, and generally contain such vegetable acids as malic, citric, tartaric, etc.

2. *Acid fruits*—lemon, gooseberry, tamarind, etc.—contain less sugar but a greater amount of acid than the preceding.

3. *Starchy fruits*—chestnuts, bread fruit.

4. *Oily fruits*—nuts of different kinds, sweet almonds, etc.

In conclusion, with regard to albuminous foods it may be stated, in general terms, *that wherever vital operations are going on there nitrogenous matter is to be found*, the operations of life occurring through its instrumentality. The nitrogenous tissues, which are the machines for living actions, have first to be constructed and then maintained. *Accordingly nitrogenous food is required for the construction as well as the maintenance of the tissues.* Hard work is best performed with an abundant supply of proteids, as this leads to a better nourished condition of the animal machine and its component parts, such as muscle and the like; and to keep up this good condition for work a liberal supply of nitrogenous food is absolutely essential. In addition to supplying the nitrogenous waste, and forming one of the great sources of fat in the economy, *the proteids excite the metabolic activity of the body*, and hence they are not stored up so readily as the fats and carbohydrates.

CHAPTER VI.

FATS, CARBOHYDRATES, AND MINERALS.

FATS AND CARBOHYDRATES.—Starch, sugar, and dextrin are easily assimilated, but the gums and celluloses are not so. In the previous chapter reference has been made to the amount of these carbohydrates and fats present in different foods. These bodies may, to a certain extent, replace the nitrogenous foods. The proteids, we have seen, can undergo metamorphoses fitting them to evolve energy, but the combustible material which evolves energy most largely and efficiently is supplied in the fats and carbohydrates; indeed, as force-producers they possess a very high dietetic value; and as great storehouses of potential energy they may be regarded as the *ultimate*, though not necessarily the *direct* sources of heat as well as of muscular energy. The potential energy of the fats, however, is much greater than that of the carbohydrates, developing more than twice as much heat.

With a fixed quantity of the fats or carbohydrates an increase in the accompanying proteid leads to an increase in the carbon consumption, owing to the proteids favoring an increase in the metabolism of both kinds of food.

As to the *rôle* played by *alcohol* in the economy there is still some difference of opinion, but the weight of evidence is in favor of the theory that it acts more or less as an aliment. When ingested in excess much of it traverses the system unburnt, and is then found in the urine, sweat, and expired air (LALLEMAND, PERRIN, etc.); but when taken in a moderate dose the amount eliminated by the urine forms but a small proportion of that absorbed (DUPRÉ); some even maintain that the quantity thus excreted does not amount to more than 0·7 per cent. (THRESH). The chief portion of the alcohol in the latter case, therefore, undergoes consumption in the body (ANSTIE, THUDICHUM, SCHULINUS, BAUDOT, &c.) We shall see elsewhere that a little alcohol is even generated in the tissues of the organism itself (BÉCHAMP).

Alcohol does not appear to increase the production of heat as a chemical agent (E. SMITH), rather in large amount lowering the temperature by checking some of the oxidations occurring in the body, particularly when abnormal, as in fevers. It also, when given in a state of health, tends to diminish muscular power, but indirectly the effect may be to increase it by improving the tone of the system through the appetite and digestion of food.

While the carbonic acid exhaled is slightly diminished when wines and beer are taken in moderate quantity, the secretion of the gastric and pancreatic juices is favored, and there is a gentle excitation of the nerve centres, and at the same time an undoubted addition made in the form of salts, fats, glycerin, and albuminoids—beer not only being stimulating and tonic, but also nutritious. Indeed, of the alcoholic drinks beers occupy the first place as foods; then come cider and perry, and then wines; and as they sustain and increase vital action they must be regarded as true foods (E. SMITH). According to VOIT also alcohol must be regarded as a food, as under its influence fewer substances are decomposed in the body.

MINERALS.—The several salines, including the extractives of animal and vegetable food, are, in a sense, quite as essential elements of a dietary as its proteids, fats, or carbohydrates. They appear to regulate in some way the energy of the food stuffs (FOSTER), a diet from which phosphorus or phosphates, chlorides, and potash or soda salts are absent, being useless for nutritive purposes. The important salts in the organism have already been referred to (p. 48), and it has been pointed out *that of the inorganic foods the most important is water*, which forms about 75 to 85 per cent. of the body weight. It is required to maintain the due bulk of the blood and other animal tissues of which it is so large a constituent, and in addition it is useful in mastication and digestion, facilitating these processes, and in keeping up the constant outpourings and reabsorptions of great volumes of liquid in the alimentary canal, and in the tissues generally, by which the body fluids, and particularly the blood, are maintained in a normal condition. It also keeps different substances in solution or suspension in the body, and serves as a vehicle to carry away waste products, and at the same time regulates the temperature of the body by its evaporation at the surface.

There is about 15 to 25 ounces of water contained in the solid food taken in the 24 hours; but besides this 60 to 70 ounces more are required.

The *remaining salts of importance* are sodium chloride, carbonate of lime, and the phosphates of potash, soda, and lime, and in smaller amount salts of magnesia, iron, and silica. If an animal is deprived of these salts they will diminish in the urine. They are required to maintain the constitution of the tissues, and they are essential in keeping up the diffusion streams in the organism. Some of the salts fulfil a special function: thus the hydrochloric acid of the gastric juice is formed at the expense of the chlorides, while the alkaline carbonates and the alkaline salts of the vegetable acids serve to neutralize the sulphuric and phosphoric acids formed in the system by the oxidation of the sulphur and phosphorus of the proteids, soda probably playing a similar *rôle*. Under normal conditions it is probable that the food contains an excess of salts; these are generally excreted in the urine, although it is possible that occasionally some of the excess may be stored up in the organism, so that at times more salts may be excreted by the urine than is taken in the food without any consequent evil results. It should be remembered that the change of food in children from one purely of milk to a mixed diet may result in a considerable deficiency of lime salts—a purely flesh diet, for example, being very poor in lime.

CHAPTER VII.

STARVATION.

LET us now briefly consider some of the changes that occur in the body when it is deprived of a sufficiency of food. By starvation the greatest loss occurs in the adipose tissue and glandular organs, as seen in the following table of VOIT'S, recording the results of starving a cat for 13 days:—

Adipose tissue	lost 97·0	per cent.	of its	original	weight.
Spleen	" 63·1	"	"	"	
Liver	" 56·6	"	"	"	
Skeletal muscles	" 30·2	"	"	"	
Blood	" 17·6	"	"	"	
Brain and spinal cord . .	" 0·0	"	"	"	

Accordingly we find that the destruction of albuminoids, when the organism is deprived of food, is determined not only by the size of the organ, but by the amount of fat present—the more the fat, so much the less destruction of albumen. This VOIT found to be the case with cats and dogs; and it holds good also with herbivorous animals, such as rabbits, the decrease of fat being correlated to an increased consumption of albumen—this being longer delayed in an animal rich in fat, but manifesting itself in a few days in lean animals, albumen alone being ultimately consumed (RUBNER). The influence of the fat KUCKEIN assumes to be exerted in restraining the solution and circulation of albuminoids, and the consequently smaller chance for their disintegration, this influence being chiefly exerted by the fat present in the juices and in the organs where the albumen disintegration occurs, and not by the fat stored up under the skin and serous membranes, etc.

According to H. RANKE, in children dying from *wasting diarrhœa*, atrophy of the various organs occurs, just as in animals dying from starvation. In OHLMÜLLER'S experiments the bones and brain lost much less weight than the other organs, but the skin decreased considerably, owing to the complete disappearance of the adipose tissue. In the normal infant there are 40 per cent. of solids, but in the atrophic only 24 per cent., the relative increase of water being due to the less amount of fat constituents, which are only 3 per cent. in comparison with 21 per cent. in the normal infant. The active organs upon which the maintenance of life depends are protected from decrease possibly at the expense of the organic albuminoids, which, becoming fluid, enter the circulation and are consumed; only when this supply fails do these organs begin to suffer loss of substance.

CHAPTER VIII.

CHEMISTRY OF THE ALCOHOLS AND FATTY ACIDS, ETC.

REFERENCE will be made to but a few of these bodies, and only so far as it concerns our present subject. For additional details the student is referred to one of the larger text books on organic chemistry.

A. The term *alcohol* is applied to compounds of hydroxyl (OH) with univalent or multivalent hydrocarbon radicles, or more simply alcohol may be looked on as water, $\left.\begin{matrix}H\\H\end{matrix}\right\}O$, in which half the hydrogen is replaced by an organic radicle; and accordingly alcohols may be regarded as the *hydroxyl substitution derivatives of the hydrocarbons*, being therefore the organic analogues of the metallic hydrates.

From propane, C_3H_8. are thus derived the three alcohols: propyl alcohol, $C_3H_7(OH)$; propenic alcohol, or propyl glycol, $C_3H_6(OH)_2$; and propenyl alcohol, or glycerin. Of the chief alcohols there are three classes; *monatomic*, as methyl alcohol, CH_3OH, and ethyl alcohol, C_2H_5OH; *diatomic*, as the *glycols*, ethyl glycol, $C_2H_4(OH)_2$, prophyl glycol, $C_3H_6(OH)_2$, and butyl glycol, $C_4H_8(OH)_2$; and *triatomic*, as glycerin, $C_3H_5(OH)_3$.

Cholesterin is a true alcohol, $\left.\begin{matrix}C_{26}H_{43}\\H\end{matrix}\right\}O$, and is probably the only one found as such in the body.

ETHYL ALCOHOL (C_2H_6O).—This is the well-known alcohol of commerce, and is chiefly obtained by the fermentation of cane and grape sugar, in which process carbonic anhydride is evolved and alcohol formed, a number of other bodies making their appearance in addition, as glycerin, succinic acid, cellulose, fats, and occasionally lactic acid.

The strongest *rectified spirit* of commerce contains 13 to 14 per cent. water, and has a specific gravity about 0·835. *Absolute alcohol*, as its name implies, is free from water; it is colorless, and has a specific gravity of 0·7938, boiling at 78·4°. *Proof spirit* has a specific gravity of 0·919, and contains 49¼ per cent. alcohol. *Methylated spirit* is a mixture of 90 per cent. spirits of wine of a density of 0·83, and of 10 per cent. partially purified wood spirit (methyl alcohol).

When alcohol is heated in a test tube, either alone or with caustic potash, it volatilizes without being blackened, its vapor having a characteristic odor and being combustible. It is not blackened when heated with sulphuric acid. When a little strong sulphuric acid is added to it, and then some dilute solution of potassic bichromate (one-third per cent.) poured into it, a green color is produced at the point of contact.

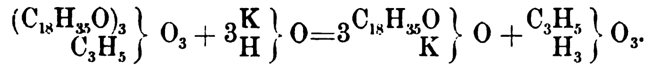
To Separate Alcohol from Organic Tissues or Fluids.—Boil for some time with water, or boil their watery extracts, and then distil. In the case of urine add tannic acid before distilling. The distillate must be rendered alkaline with caustic potash and again distilled. This last distillate is acidified with sulphuric acid and distilled for a third time, when all the alcohol will be present in the receiver. It may be rendered anhydrous by distilling it once again after saturation with quick lime or potassium carbonate.

With vomited matter, or where much alcohol is present, it is advisable to make a series of distillations after successive additions of sodium chloride to the fluid in the receiver.

To determine quantitatively the alcohol is first transformed into acetic acid, and this determined volumetrically. To effect this conversion sulphuric acid and some potassic bichromate solution (one-third per cent.) are added to the fluid, and the whole heated for two hours in a water or sand bath at 80° to 90°. The resulting acetic acid is distilled out and the distillate titrated with standard soda solution.

GLYCERIN (**Propenyl Alcohol**), $C_3H_8O_3$ or $\left.\begin{matrix}C_3H_5\\H_3\end{matrix}\right\}O_3$.—This is a triatomic alcohol which forms a nearly colorless, viscid, and very sweet syrupy liquid that is very hygroscopic and very soluble in water and alcohol, but insoluble in ether. At 15° it has a specific gravity of 1·26, begins to evaporate at 100°, and boils at 290°; it forms a gummy mass at —40°, and crystals have been obtained of it belonging to the rhombic system. Glycerin dissolves up, especially with the aid of heat, the oxides of copper and lead and of the alkali metals, etc.; the fatty acids, iodine, and many organic bodies, such as cholesterin and uric acid, are also dissolved by it, and it acts as a particularly good solvent for the ferments. Glycerin oxidizes easily in the air, and rapidly reduces silver nitrate.

Preparation.—It is obtained in the saponification of fats by caustic alkalies, or by the decomposition of these bodies by superheated steam. When stearin is boiled with caustic potash a stearate is formed, and glycerin is set free:



$$\left.\begin{matrix}(C_{18}H_{35}O)_3\\C_3H_5\end{matrix}\right\}O_3+3\left.\begin{matrix}K\\H\end{matrix}\right\}O=3\left.\begin{matrix}C_{18}H_{35}O\\K\end{matrix}\right\}O+\left.\begin{matrix}C_3H_5\\H_3\end{matrix}\right\}O_3.$$

(tristearine) (potassic stearate)

The formation of glycerin may be shown on a small scale by mixing a little fat with some finely powdered plumbic oxide and water, and then heating; a lead plaster is formed and glycerin remains in solution in the water, Filter and pass a current of sulphuretted hydrogen through the liquid, evaporate to a small bulk, and filter again.

Combinations, Etc.—Combined with the different fatty acids it constitutes a large part of animal and vegetable fats. In the free state it may be met with in small quantities only in the intestines, as the result of the action of pancreatic juice on the fats. When heated with acetic and benzoic acids, etc., it forms compound ethers; these glyceric ethers or glycerides are mostly oily, but those formed by the higher fatty acids, as palmitic and stearic are solid fats. Most fats and oils are mixtures of ethereal salts formed from glycerin and acids of the acetic and oleic series. With chlorine, bromine, and iodine it forms substitution compounds; and at high temperatures and pressures it enters into combination with certain inorganic acids, as glycerin-sulphuric acid, $C_3H_5\left\{\begin{matrix}OH\\OH\\SO_4H\end{matrix}\right.$, glycerin-phosphoric acid, $C_3H_5\left\{\begin{matrix}OH\\OH\\PO_4H_2\end{matrix}\right.$, and trinitrin or nitroglycerin, $C_3H_5(NO_3)_3$.

Detection.—Evaporate the liquid to be tested after the addition of caustic lime and sand. The powdered residue is exhausted with a mixture of equal parts of alcohol and ether, the solvent removed by evaporation, and the residue heated very carefully to 120° with two drops of phenol and the same quantity of strong sulphuric acid. The melt is treated with a little water, and the insoluble residue rendered slightly ammoniacal, when the beautiful red coloration of glycereïn will appear.

B. Closely allied to the alcohols are the *acids*, which are readily obtained from them by oxidation. The monatomic alcohols ($C_nH_{n2+2}O$, or $C_nH_{2n+1}OH$) give origin to the *monobasic acetic acid series* ($C_nH_{n2}O_2$), as formic acid, CH_2O_2 or $HCHO_2$. In this conversion by oxidation it may be assumed that the CH_2OH group has been changed into the carboxyl or $COOH$ group. The diatomic alcohols or glycols [$C_nH_{2n+2}O_2$ or $C_nH_{2n}(OH)_2$] by their oxidation give rise to two series of acids, the *glycollic* ($C_nH_{2n}O_3$) and the *oxalic* ($C_nH_{2n-2}O_4$). Thus ethene alcohol or ethyl glycol treated with nitric acid gives up 2 or 4 of its hydrogen atoms in exchange for oxygen, according as the oxidation occurs at a low or high temperature, glycollic or oxalic acid being produced; as

$$\underset{\text{(ethyl glycol)}}{C_2H_4(OH)_2}+O_2=\underset{\text{(glycollic acid)}}{C_2H_4O_3}+H_2O$$

$$C_2H_4O_3+O_2=\underset{\text{(oxalic acid)}}{C_2H_2O_4}+H_2O.$$

Of the *glycollic* or *lactic series* the important members, physiologically speaking, are carbonic (H_2CO_3), glycollic ($HC_2H_3O_3$), and lactic ($HC_3H_5O_3$) acids. With the exception of the carbonic they are all monobasic.

The important members of the *oxalic series* to which reference will be made are oxalic ($H_2C_2O_4$) and succinic ($H_2C_4H_4O_4$) acids. These are all dibasic.

I. *The fatty or acetic acid series.*

Formic acid	CH_2O_2	or $CHO.OH$.
Acetic “	$C_2H_4O_2$	“ $C_2H_3O.OH$.
Propionic “	$C_3H_6O_2$	“ $C_3H_5O.OH$.
Butyric “	$C_4H_8O_2$	“ $C_4H_7O.OH$.
Valerianic“	$C_5H_{10}O_2$	“ $C_5H_9O.OH$.
Caproic “	$C_6H_{12}O_2$	“ $C_6H_{11}O.OH$.
Palmitic “	$C_{16}H_{32}O_2$	“ $C_{16}H_{31}O.OH$.
Stearic “	$C_{18}H_{36}O_2$	“ $C_{18}H_{35}O.OH$.

FORMIC ACID, $CHO.OH$, has been found in several organs and fluids of the body, such as the spleen, pancreas, thymus, and brain, and in the juice of muscle. In leukæmia it is more generally spread, and may present itself in the blood, urine, sweat, and marrow.

It is *obtained* by the oxidation of organic substances in general, such as sugar and starch. Formic acid acts as a powerful reducing agent, as can be shown by heating it with silver or mercuric salts; and it may be regarded as one of the excretory products of tissue change, though it is in great part further burnt to carbonic anhydride and water.

ACETIC ACID, $C_2H_3O.OH$ or $CH_3CO.OH$, is a colorless liquid, the strongest form solidifying to an ice-like mass below 15°, and hence the name *glacial* applied to it.

It is present in the juice of muscle and of many glands, as the spleen, etc.; also in bile and sweat, and in the stomach and intestine as the result of fermentations, especially after the ingestion of sugar and starch, particularly in catarrhal condition of the mucous membrane. The glacial acetic acid is prepared by distilling sodic acetate with strong sulphuric acid.

Acetic acid forms *normal or neutral acetates*, as $KC_2H_3O_2$; and *acid* salts, as $KC_2H_3O.C_2H_4O$. With lead the following salts are formed: *normal acetate*, or sugar of lead, $Pb(C_2H_3O_2)_2$, which is soluble in alcohol and slightly soluble in water; and the ***basic salts*** or ***subacetates:*** sesquibasic acetate (Goulard's extract), $2Pb(C_2H_3O_2)_2PbO$; triplumbic acetate, $Pb(C_2H_3O_2)_2 2PbO$, obtained by mixing a cold saturated solution of the normal salt with a fifth of its volume of ammonia; and ***sexplumbic acetate***, $Pb(C_2H_3O_2)_2 5PbO$, formed by adding a great excess of ammonia to a solution of the normal salt.

Test.—It gives a red color, but no precipitate, with ferric chloride (Fe_2Cl_6), but this color is discharged by hydrochloric acid. The same red coloration is also given with formic, pyrogallic, sulphocyanic, and meconic acids. But the *formic* and ***pyrogallic acids*** precipitate silver nitrate solutions with reduction of metallic silver, and the pyrogallic acid gives also a blackish blue coloration with ferrous sulphate. The red coloration given by ***sulphocyanic acid*** is discharged by mercuric chloride, but not by hydrochloric acid, while that given by ***meconic*** acid is removed by neither of these bodies.

To ***separate acetic acid*** the general plan may be adopted of making two distillations of the liquid containing it, the first being made after the addition of a few drops of sulphuric acid, and the resulting distillate then saturated with carbonate of soda, evaporated to dryness, and again submitted to distillation after being dissolved up in dilute sulphuric acid. Formic acid may be present in the distillate, but it can readily be separated by boiling the distillate with mercuric oxide, which decomposes the formic acid.

PROPIONIC ACID occurs sometimes in the sweat, and occasionally in fermenting diabetic urine, and in the intestinal tract; it has also been described as present in the blood in leukæmia and in the vomited matters in cholera.

BUTYRIC ACID.—Two modifications are known—normal or fermentation-butyric or ethyl-acetic acid, and isobutyric or dimethacetic acid.

It is found free in the sweat and as a triglycerid in butter; it is also met with in the fæces and urine, in the juice of muscle and of many glands, and in various kinds of decomposing animal and vegetable matter. *Pathologically* it appears in the free state in the stomach, urine, blood, fluid of ovarian cysts, and in the sputa in gangrene and bronchiectasis of the lung. It occurs in the organism together with lactic acid, in consequence of putrid fermentations of starches or saccharine bodies.

Butyric acid is a viscid liquid that burns with a blue flame, and is easily soluble in water, alcohol, and ether, calcic chloride separating it from its solutions as an oily liquid. It is precipitated by sulphate of copper and hydrate of baryta, and gives a yellow precipitate with nitrate of silver ($C_4H_7AgO_2$), and salts of lead and zinc also combine with it.

VALERIANIC ACID is often present in the fæces and is an oily liquid. Valerianate of ammonia is produced in the putrefaction of impure leucin, and accordingly it may be met with in the urine in acute atrophy of the liver, and in typhus and variola.

CAPROIC ACID is an oily fluid contained in butter; it occurs in fæces after a meat diet, and is occasionally also to be found in sweat. It is produced, together with other acids of the fatty series, by the oxidation of albuminous substances and of the higher fatty acids.

The palmitic and stearic acids are insoluble in water, readily soluble in ether, chloroform, or hot alcohol, soluble also in glacial acetic acid. They enter into the composition of nearly all vegetable and animal fats, forming glycerides, and combine with the alkalies to form soaps, the latter generally consisting of mixtures of the potash and soda salts of these and other fatty acids, the soda soaps being known as the hard and the potash soaps as the soft soaps.

PALMITIC ACID ($C_{15}H_{31}CO.OH$) is a colorless solid body, crystallizing in beautiful white needles, or in masses of crystalline scales when it cools after having been melted. It forms three ethers or palmitins—monopalmitin, $C_3H_5\left\{\begin{matrix}(OH)_2\\(C_{16}H_{31}O_2)\end{matrix}\right.$; dipalmitin, $C_3H_5\left\{\begin{matrix}OH\\(C_{16}H_{31}O_2)_2\end{matrix}\right.$; and tripalmitin, $C_3H_5(C_{16}H_{31}O_2)_3$. Palmitic acid is occasionally met with in decomposing pus, cheesy tubercle, and sputa in gangrene of the lung.

STEARIC ACID is the chief constituent of the more solid animal fats, as suet and the like; but it is also abundant in the softer fats, as in human fat and butter. It crystallizes in large glancing scales, and, like palmitic acid, it forms stearic ethers or stearins. It is generally found mixed with palmitic acid, though this latter may be chiefly present, as in palm oil, but they can be separated by dissolving the mixture in hot alcohol and adding to this an alcoholic solution of acetate of magnesia; magnesic stearate crystallizes out, which can then be decomposed by hydrochloric acid. By heating the separated stearic acid again with hydrochloric acid, and crystallizing it several times from alcohol, the stearic acid can be obtained in moderate purity.

II. Of the glycollic series we shall only refer to **LACTIC ACID,** $C_3H_6O_3$, which forms a syrupy colorless liquid, soluble in water, alcohol, and ether. Two or three of its four isomeric modifications exist in the body. As *ethylidene-*, *fermentation-*, or *iso-lactic acid* it is obtained in lactic acid fermentation, and the same form is met with in the intestinal tract, occurring also in many glands and in ganglionic nerve cells. *Ethylene lactic acid* generally accompanies *ethidene-*, *para-*, or *sarco-lactic acid* in the watery extract of muscle, but with regard to its presence there is still some doubt, although it is said to have been found also in certain pathological exudations (WISLICENUS). The *sarco-lactic acid* appears in muscles, especially after prolonged activity, also in the hepatic cells. It differs from ordinary lactic acid in polarizing light largely, the free acid being dextro- and the anhydride lævo-rotatory; and in its salts crystallizing differently, and with a smaller proportion of water.

Abnormally lactic acid is met with in the blood, particularly in leukæmia, pyæmia, puerperal fever, and may show itself in purulent discharges, in the saliva in diabetes, and in the urine, especially after phosphorus poisoning, in acute atrophy of the liver, leukæmia and trichinosis, and occasionally in osteomalacia and rickets.

Preparation.—Dissolve cane sugar, 3 kilo., in 13 litres boiling water, and add 13 grams tartaric acid; and after several days mix with this 4 kilo. sour milk with which has been stirred up 100 grams old cheese and 1·5 grams carb. of zinc. Leave for eight days at 30° to 35°; collect the deposit of lactate of zinc and crystallize it out of hot water; dissolve it up again in boiling water, and pass a current of sulphuretted hydrogen through the solution. The filtrate is then to be evaporated to a thin syrup and shaken up with ether, and the ether extract distilled off over a water bath.

(See the preparation of sarcolactic acid under Muscle.)

Lactic acid is possibly a derivative in the organism of sugar: $C_6H_{12}O_6 = 2(C_3H_6O_3)$. Its decomposition into carbonic acid and water is easily effected in the system, although it may at first be split into butyric acid, carbonic acid, and hydrogen (HOPPE SEYLER).

A watery solution of lactic acid, when exactly saturated with caustic soda, will after some time again show an acid reaction. A similar solution also possesses the property of suddenly diminishing in its specific rotatory power on light when diluted, this gradually rising again, but never to its original amount. If boiled with carbonate of lime, *lactate of lime*, $2[(C_3H_5O_3)_2Ca]+9H_2O$, separates in tufts of fine needles. *Lactate of zinc*, $Zn(C_3H_5O_3)_2+3H_2O$, is obtained in crystalline needles or crusts: it is insoluble in alcohol, but is slightly soluble in water, the paralactate being much more soluble than the ordinary lactate. It also forms little silky needles when boiled with carbonate of silver; this *silver lactate* is almost insoluble in cold, but easily soluble in hot alcohol, and if long boiled the alcoholic solution takes a blue color.

III. Of the oxalic series we shall describe the two following:—

OXALIC ACID, $C_2H_2O_4$ or (COOH)(COOH), only exists in the body in a combined form, principally as *oxalate of lime* (CaC_2O_4). The characters of this body are given under urinary deposits. In this form also it exists ready formed in many plants, often separating out of their juice in microscopic octahedral crystals, and after the use of these vegetables it may appear abundantly in the urine. It is also abundant in the urine in chronic catarrh of the bladder and in different mucous inflammations, and occasionally it is found in the mucous membrane of the gall bladder and uterus. It is possibly held in solution in the urine, before being deposited, by the urates and acid sodic phosphate (NEUBAUER). But oxalate of lime can also be built up in the organism. An injection of urates into the blood increases the oxalate of lime in the urine, so that it is possible for the oxalic acid to originate in the organism from uric acid; but under normal conditions, when active oxidation is going on, oxalic acid rarely appears, being burnt off to carbonic acid and water. An oxalate to which a little powdered black oxide of manganese is added, then a little water and a few drops of sulphuric acid, evolves carbonic acid.

SUCCINIC ACID, $H_2C_4H_4O_4$ or $\left\{\begin{matrix} CH_2CO.OH \\ CH_2CO.OH \end{matrix}\right.$—It is found in the spleen, thymus and thyroid; occasionally in urine, especially after eating asparagus and the malic acid of fruits; also in the fluid of echinococcus cysts, and in the serum of hydrocele and hydrocephalus; MEISSNER has met with it in the blood and saliva, and in the free state it may appear in the stomach and in active muscle juice. When oxidized by nitric acid, all the acids of the fatty series, from the butyric upwards, yield succinic and other similar acids.

It crystallizes in large rhombic tables or prisms, occasionally forming prismatic needles or hexagonal plates; and is soluble in 3 parts boiling and 17 parts cold water, less soluble in alcohol and insoluble in ether; it begins to sublime at 120°, melts at 180°, and decomposes at its boiling point, 235°.

Succinic acid is formed by the oxidation of many organic substances, especially the fatty acids, and it may possibly be a derivative of proteid decomposition. Ferric chloride gives with it a brown flocculent precipitate; and it is also precipitated by neutral acetate of lead, and by salts of silver and mercury.

IV. Only two other bodies will be here described, to complete this very cursory sketch of the alcohols and organic acids—namely, oleic acid and phenol.

OLEIC ACID belongs to the acrylic series, of which the general formula is $H(C_nH_{2n-3})O_2$. It is monobasic, $HC_{18}H_{33}O_2$ or $C_{18}H_{33}O.OH$. When heated with caustic potash it breaks up thus: $C_{18}H_{34}O_2+KHO=C_2H_3KO_2$ (potassic acetate) $+C_{16}H_{31}KO_2$ (potassic palmitate) $+H_2$. This acid is found in all the fats of the body, and is present also in most natural fats and non-drying oils. It forms a clear oily liquid that is insoluble in water, but readily soluble in alcohol and ether, and crystallizes in white needles which melt at 14°.

Like the palmitic and stearic acids it forms three glycerides. By heating it we obtain silky needles of sebacic acid ($C_{10}H_{18}O_4$); and it forms a neutral oleate with lead, which is distinguished from the plumbic salts of the other fatty acids by its solubility in boiling alcohol.

PHENOL (**Carbolic Acid, Phenic Acid**), C_6H_6O or C_6H_5OH, belongs to the benzine group, C_6H_6. This body is produced in the dry distillation of coal, forming the chief constituent of the acid part of crude coal-tar oil; by the dry distillation of salicylic acid it is also readily prepared.

The urine of the horse and cow normally contains it, and in human urine it is present after the administration of benzine. It seldom presents itself in the urine in the free state, but frequently as phenyl sulphate ($C_6H_5OSO_3H$) and hydrochinon [$C_6H_4(OH)_2$]. The dark color of the urine after the ingestion or absorption of this acid is probably due to the oxidation of the hydrochinon or its isomer, brenzcatechin, derived from it (BAUMANN).

Under normal conditions the amount present is very slight, but it is increased in certain diseases, especially those where the intestinal contents are retained, as in ileus, though it has also been found even in cases of diarrhœa with rapid decomposition of the intestinal contents. Part of the phenol at least is probably derived from some of the decomposition processes occurring to the proteids in the intestine.

It forms a colorless, oily liquid, boiling at 183° and solidifying at low temperatures, crystallizing in large colorless prisms which fuse at 37·5°; its solubility in water is very slight (1 : 20), but it is very soluble in alcohol, ether, and potash.

To detect the acid in the urine this liquid should be distilled after the addition of some alkaline carbonate, and the tests can readily be applied to the first portions of the distillate.

Tests and Properties. 1. Perchloride of iron gives with it a deep violet color, which quickly changes to a dirty brown.

2. A chip of fir or a deal shaving moistened with a watery solution of carbolic acid, then plunged in dilute *hydrochloric acid* and exposed to the light, is tinged of a deep greenish blue.

3. *Nitrate of Silver* is reduced by it, and it is transformed into picric acid by long boiling with strong *nitric acid*, oxidizing with violence and forming a red solution, which on cooling deposits yellow crystals.

4. Add to a watery solution quarter its volume of *ammonia*, then some drops of *potassium chloride* solution (1 : 20), and warm gently; a beautiful blue color will soon appear, or, if the solution is very dilute, the color will be more or less greenish.

5. Gives a blue coloration in presence of a little *anilin* and an alkaline solution of *sodic hypochlorite;* this is a very delicate reaction (JACQUEMIN).

6. A dilute watery solution gives a yellowish white crystalline precipitate of tribromphenol ($C_6H_2Br_3OH$) with *bromine water.* Salicylic acid gives a similar precipitate, so that in testing urine for carbolic acid in presence of this acid we should neutralize with carbonate of soda and shake up with ether, which removes the phenol. This method may be employed in the quantitative determination of carbolic acid, 331 parts of the bromine being equivalent to 94 of the acid.

7. Boil a little very dilute solution with Millon's reagent, and an intense red coloration is produced.

8. Add a little carbolic acid to yellow nitric acid or to a solution of potassic nitrite (6 per cent.) in strong sulphuric acid, and a brown color is produced, changing to a green and then to a blue.

CHAPTER IX.

CHEMISTRY OF THE CARBOHYDRATES.

To the carbohydrates belong the starches, dextrin, and sugar. They may be thus grouped:—

I. *Glucoses.*	II. *Saccharoses.*	III. *Amyloses.*
$C_6H_{12}O_6$.	$C_{12}H_{22}O_{11}$.	$n(C_6H_{10}O_5)$.
Grape sugar, or dextrose.	Cane sugar.	Starch.
Galactose.	Lactose, or sugar of milk.	Dextrin.
Inosit.	Maltose.	Glycogen.
Lævulose, or sugar of fruits.	Arabin (in gum arabic).	Cellulose.
		Granulose.

The glucoses are regarded by some authorities as the aldehydes of the natural sugars or hexhydric alcohols, mannite and dulcite, the former present in manna, an exudation from a species of ash, and in the sap of the apple and cherry, and the latter in the berries of the mountain ash. These two bodies have the composition $C_6H_8(OH)_6$, but they do not ferment or reduce an alkaline solution of a cupric salt. By the action of nascent hydrogen grape sugar is converted into mannite, and by acting in the same way on inverted milk sugar dulcite has been obtained. Of the diglucosic alcohols or saccharoses, $2C_6H_{12}O_6—H_2O=C_{12}H_{22}O_{11}$, we have examples in cane and milk sugar. Further, there are anhydrides of the glucoses ($C_6H_{12}O_6—H_2O=C_6H_{10}O_5$), or the so-called amyloses. They all belong to the carbohydrates, as they consist of 6 or 12 atoms of carbon united with hydrogen and oxygen in the proportion in which they form water (H_2O).

STARCH (Fecula, Amidin), $n(C_6H_{10}O_5)$, or taking $n=3$, then $C_{18}H_{30}O_{15}$.—This body is most widely diffused throughout the vegetable kingdom, being found in nearly every plant, and as a rule most abundantly in certain roots and tubers, soft stems, and seeds.

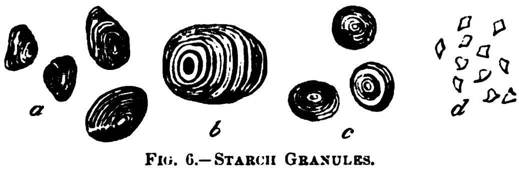


FIG. 6.—STARCH GRANULES.

a, potato starch; *b*, potato starch highly magnified; *c*, wheat starch, rings not so well marked as in the potato; *d*, rice starch, very small and angular.

It appears as a white glistening powder that is made up of little rounded transparent bodies or granules, each of which has a central spot or hilum around which are a series of depressed more or less parallel rings. These granules vary in appearance according to their source. Each granule consists of an outer layer of cellulose enclosing alternating layers of granulose and cellulose. A variety of granulose present in small amount and giving a red color with iodine BRÜCKE has named erythrogranulose.

Starch is nearly insoluble in cold water and most liquids. When it is boiled with water the granules of which it consists burst and disappear, but even with much water the starch is chiefly suspended as a colorless jelly, only a small proportion being in solution.

Conversion of Starch into Sugar.—Make a thick, gelatinous, starchy solution, and add to it a little lukewarm watery infusion of malt; heat the mixture to about 70°, and in a few minutes the thick, gelatinous starch gives place to a thin fluid containing dextrin and glucose. The infusion of malt acts by virtue of the presence in it of the ferment diastase; the temperature must not, therefore, rise as high as 100°, or the ferment will be rendered inactive. When starch is converted into sugar by the action of acids or diastase, dextrin and glucose are formed simultaneously (MUSCULUS): $C_{18}H_{30}O_{15}+H_2O=C_6H_{12}O_6+2C_6H_{10}O_5$. The dextrin obtained by the action of saliva on starch BRÜCKE regards as a mixture of *erythrodextrin*, colored red by iodine, and *achroodextrin*, which is not colored, and is possibly not converted into sugar at all, or if so with difficulty.

LEUCHS first demonstrated the conversion of starch into sugar *by means of saliva*, the active principle of which is ptyalin, 1 part of this body being capable of converting 2,000 parts of starch into sugar.

Raw starch is more slowly acted on than starch that has been cooked, raw maize starch, however, being changed in a few minutes, but raw potato starch very slowly; and all starches are not affected alike, for boiled potato starch is more easily converted into sugar than boiled wheaten starch, and this in turn more quickly than rice starch (LEFBERG). Further, the cellulose is not so readily, if at all, converted into sugar by the saliva as the granulose; therefore when the cellulose coats are ruptured by boiling the granulose is more easily acted on.

Starchy substances *to serve as nutriment* must first undergo this change into glucose by the action of animal diastase, a ferment found not only in the saliva, but also in the pancreatic and intestinal juices; its digestion, accordingly, commences in the mouth, where a certain amount of sugar is formed; it also continues in the stomach, but to a less extent, on account of the acidity of the gastric juice, the presence of albumen, however, not interfering with the conversion in any way (MIALHE), although it affects the reduction of cupric oxide when the copper test is employed to detect the presence of the sugar. In the small intestine the diastatic conversion occurs with renewed energy from the afflux of the fresh ferment of the pancreatic and intestinal juices, the acid reaction at the same time gradually disappearing.

Starch is a colloid. To fit it for absorption it must therefore be changed into sugar. Take two large glass tubes about 3 inches wide (students may also make use of small funnels), and tie very firmly a piece of moist parchment or of the large intestine of a sheep over one end of each; then, having nearly filled them both with water holding some cooked starch in suspension, and added to one of them a little saliva, fix them vertically in two dishes. Lay them aside for 12 hours in a moderately warm place; then test the fluids that have transuded with iodine and Fehling's solution (see p. 79): sugar will be detected in the fluid that has come from the tube to which saliva was added, but no starch will be found in either transudation.

Starch, therefore is a colloid, and does not pass through animal membranes, whilst sugar readily does so; and the sugar in this experiment has been derived from the conversion of some of the starch by the saliva.

Tests.—1. Add *tannic acid* to a solution of starch: a yellow precipitate containing tannic acid falls down, which redissolves on the application of heat.

2. *Free iodine* forms a deep indigo-blue compound with starch, but heat destroys the color if long applied. Some dilute solution of iodine is added to a little starch mucilage (see their preparation, p. 34) in a test tube, or starch granules on a microscopic slide are irrigated with the iodine solution. This is done as follows: Spread a small pinch, say of potato starch, or a scraping of the cut surface of a raw potato, upon a slide in a drop of water, apply a cover glass, and then place a drop of the iodine solution on one side of the cover glass and a slip of filter paper close to the other side. Very soon the iodine solution finds its way inwards, and stains the starch granules a beautiful blue. Before the cellulose constituent takes this blue color it must first be acted on with sulphuric acid or chloride of zinc.

DEXTRIN (**British Gum**) is intermediate between starch and sugar. It is the name given to the body obtained by boiling starch paste with a little dilute sulphuric or hydrochloric acid until the paste becomes thin and limpid and more or less gumlike; but if the boiling is too long continued dextroglucose will be formed. It is also obtained by heating dry potato starch up to 400°, when the latter becomes yellowish and soluble in water. Diastase effects the same thing with starch paste, although its continued action leads to the formation of maltose.

Dextrin has been found in the blood and organs of herbivora, and LIMPRICHT has discovered it in the flesh of young horses and dogs, probably as a decomposition product of glycogen, and occasionally in the liver; REICHARD found it once in diabetic urine, and it appears in the alimentary canal after the ingestion of starch.

It is a gummy-like body, forming a white or yellowish powder, which is soluble in water, constituting a turbid solution, but insoluble in alcohol and ether; it does not reduce cupric oxide (or only to a slight extent), nor does it ferment with yeast, but it has a strong right polarizing action on light, and is readily converted by the action of dilute acids or diastase into grape sugar. With a watery *solution of iodine it gives a brownish or port-wine red color*, which disappears on heating.

BRÜCKE, as we have seen, distinguishes two kinds of dextrin—*erythrodextrin*, whose solution is colored of a rosy red by iodine, and *achroodextrin*, which is not colored by it, and is not so readily converted into sugar, although this change may be effected by boiling it with dilute hydrochloric acid. The dextrins possess many points of resemblance to glycogen, which polarizes in the same way and is similarly acted on by acids and ferments; but while neutral watery solutions of dextrin are transparent those of glycogen show an intense white opalescence; iodine solution also stains glycogen of a dark brownish and not of a rosy red, as is the case with dextrin.

Tests.—Alcohol precipitates it from its aqueous solutions, so also does *lime water*, and a mixture of *ammonia and basic acetate of lead;* when boiled with *nitric acid* it yields oxalic acid. Its solutions give a violet coloration with a solution of iodine in potassic iodide. Boil a few minutes with dilute hydrochloric acid; the solution becomes thinner, and gives the tests for grape sugar.

It is *distinguished from starch* by its amorphous shape and its red coloration by iodine, and *from glycogen* by the want of opalescence of its solutions and by its not being precipitated by basic acetate of lead alone.

To prepare it, make 20 grams starch into a paste with 30 c.c. water, and add slowly to it 5 grams strong sulphuric acid diluted with 30 c.c. water. After mixing well, heat for some time over a water bath at about 90°. When it cools precipitate the dextrin formed by the addition of alcohol; or the sulphuric acid may be removed by saturation with chalk and subsequent filtration, the filtrate being evaporated to dryness.

CHAPTER X.

GLYCOGEN.

GLYCOGEN, $nC_6H_{10}O_5[5(C_6H_{10}O_5)$ or $11\ (C_6H_{10}O_5)$, HOFMANN; $C_{18}H_{30}O_{15}+4H_2O$, ABELES].—This body was first discovered in the liver by CLAUDE BERNARD. It is there built up by the liver cells, appearing as little granules or amorphous masses, its amount depending greatly on the character of the food; one of the great functions of this organ, indeed, being its production—this occurring even in severe diabetes (KÜLZ). The liver of young beasts is richer in glycogen than that of older animals. It is present in considerable quantity in most of the embryonic tissues, appearing to increase up to the middle period of gestation, and then gradually to diminish towards its conclusion. Glycogen would therefore appear to have an important *rôle* to play in the development of the tissues. It is also met with in all developing embryonic cells, and in the leucocytes and pale corpuscles during their period of activity. SALOMON has found it in both arterial and venous blood, and traces of it are to be met with in most of the organs, as in the pancreas, kidneys, brain, and testes, as well as in the placenta. It is constant in muscle, and in the muscles of a rabbit NASSE obtained 0·47 to 0·94 per cent., and it appears to be increased in the muscles mostly by whatever increases the formation of glycogen in the liver. With regard to muscle BRÜCKE and WEISS affirm that in tetanized frog's muscles less glycogen is present than in the resting muscles, thus pointing to a consumption, probably indirect, of glycogen during muscular contraction; there is less also in muscle when it has passed into *rigor mortis* (NASSE), but, on the other hand, the glycogen is increased when the muscle is brought into a state of paralysis by the division of its nerves (CHANDELON).

Preparation (BRÜCKE'S *Method*).—Rapidly decapitate a large and well-fed rabbit about two hours after a full meal. Open the abdomen without delay, and having torn out the liver, cut it into a few pieces and throw them into a large porcelain dish containing water that is vigorously boiling. Let them lie in the boiling water a few minutes until they are quite hard, then remove them, and after having rubbed them into a paste in a mortar return the fine pulp to the boiling water, and boil again for about half an hour, when the milky extract is to be poured off, and a fresh extraction made with more boiling water.

So far two operations have been performed: the action of the ferment has been destroyed, and a watery extract has been obtained of the liver; but as this extract contains albuminous bodies in solution, these must be precipitated. To effect this the hot extracts are to be rapidly filtered into a large beaker that has previously been inserted in a freezing mixture of snow or ice and salt, and when it has cooled hydrochloric acid and potassio-mercuric iodide solution are added to it alternately until no further precipitate occurs. The albumens are thus thrown down. Stir well and filter after five to ten minutes have elapsed, and to the filtrate add spirit until about 60 per cent. of absolute alcohol is present in the mixture; the glycogen will thus be precipitated in a tolerably pure form, which will not be the case if a larger excess of alcohol is added. The precipitated glycogen is next to be collected on a filter and washed with spirit (60 per cent.) until the washings give no turbidity with a mixture of dilute caustic potash, ammonia, and ammonium chloride; then with absolute alcohol, and repeatedly with ether. Now detach the glycogen from the filter, and dry it rapidly on a piece of porous earthenware at a moderate heat. It should form a white powder that may be further purified, if necessary, by dissolving it in hot water and precipitating it therefrom with alcohol to which a little ammonia has been added, redissolving as before, precipitating with spirit containing acetic acid, and washing this last precipitate with absolute alcohol and ether, and then drying it.

The *potassio-mercuric iodide* is prepared by carefully precipitating a saturated solution of potassic iodide with one of mercuric chloride, and having washed the resulting precipitate, making a saturated solution of it in some hot solution of potassic iodide.

Different other methods have been proposed, such as the use of caustic potash and acetic acid to separate the albumen, but the author much prefers BRÜCKE'S to any of them. It should be remembered that wherever glycogen is met with in the body a diastatic ferment can also be obtained, so that in the preparation of glycogen this should be guarded against, as otherwise much of the glycogen may be converted into sugar if the action of the ferment is not destroyed.

Properties.—It is a white or yellowish white, tasteless, inodorous, and amorphous powder, that is insoluble in alcohol or ether, but forming an imperfect opalescent solution in boiling water, which polarizes to the right about three times as powerfully as does grape sugar. In many of its properties it corresponds to dextrin (see p. 67), and when a glycogen solution is boiled part of it is changed into a dextrin-like body.

Sources.—Glycogen is very abundant in the liver after ingestion of starch and sugar, this organ, however, being comparatively poor in it after a diet of fat and albumen; but the formation of glycogen does not appear to be directly dependent on the presence of carbohydrates in the intestine; it rather seems to be an intermediate decomposition product of albumen in the organism (WOLFFBERG, etc.)

It ought to be remembered in discussing the different experiments, and the deductions therefrom as to the action of various bodies in increasing the formation of glycogen, that it does not necessarily follow that the body thus introduced becomes *directly* converted into glycogen, but that it may merely contribute indirectly by protecting the glycogen from change (TIEFFENBACH, etc.) And, indeed, for this very reason, and although the increase in glycogen is not so great after an albuminous diet, many authorities regard the carbohydrates as not going directly to the formation of glycogen, but as contributing indirectly thereto by saving albumen by their own combustion, and thus allowing more of this body to remain to be converted into glycogen. It is probable that one of the great seats of urea formation is the liver (CYON), and in diabetes we find the excretion of urea to be also increased, pointing to the probable decomposition of albumen in the liver into sugar or glycogen and urea. The proteid may also split up in the liver into glycogen and the biliary acids, or its glycocin derivative may split into urea and glucose ($4C_2H_5NO_2=2CON_2H_4+C_6H_{12}O_6$). The formation of glycogen in the liver, as well as the separation of sugar, can be markedly influenced. Thus puncture of the floor of the fourth ventricle at the point of the calamus scriptorius after a short time causes sugar to appear in the urine. And that the liver is concerned in this is seen from the fact that if the liver contains no glycogen (as after long fasting, or when its glycogenic activity is destroyed by arsenical poisoning) no sugar appears in the urine after the experiment (LUCHSINGER).

The state of the vasomotor nerves of the liver appears to exercise considerable influence on the formation of sugar. It is probably by their action on these nerves that such bodies as curara, amyl nitrite, ether, and chloral hydrate act in causing sugar to appear in the urine. It would appear therefore that diabetes is really a disease of the nervous system; but even in this disease the liver does not appear to have lost its power of forming glycogen out of sugar.

The assimilation of starches, sugars, inulin, glycerin, albumen of egg, fibrin, and casein causes an accumulation of glycogen in the liver, while inosite, quercite, mannite, glycocin, gums, and fats fail to do so (MERING, etc.)

While BERNARD obtained an increase of glycogen with a flesh diet, very little increase has been obtained by feeding animals with fibrin (DOCK, LUCHSINGER); but FINN, MERING, etc., caused its increase upon a diet of flesh or egg albumen, as well as of blood fibrin. WOLFFBERG, by feeding an animal with 8 grams albumen and 60 grams sugar daily, obtained 0·474 gram glycogen; with 30 grams albumen and 60 grams sugar, 0·821 gram glycogen; and with 50 grams albumen and 60 grams sugar, 1·84 gram glycogen in the liver. FORSTER, by an injection of glucose into the portal vein, also increased the glycogen.

Hunger is very slow in diminishing the glycogen in the liver, six days at least being required to reduce it to a minimum. It is also much exhausted by fevers. KÜLZ found that in fasting animals starch and sugar caused glycogen to appear in the liver; further, that severe exercise reduces this practically to nothing, and that five or six hours' exercise will produce a result that can otherwise be obtained only by starving the animal for twelve to twenty days.

Destination.—Glycogen must be regarded, however derived, as a store of carbohydrate material, which is used up according to the needs of the economy.

BERNARD believes that a continual conversion of this body into sugar is going on in the liver, and that the sugar formed is carried thence into the circulation, to be burnt up in the lungs and tissues generally, but particularly in the muscles. The quantity of sugar in the blood is small but constant, and, as it is constantly being used up by some of the tissues, it is possible that the supply is maintained by a regulated conversion of the glycogen. The blood of the hepatic vein is rich in sugar (BERNARD), though this is denied (PAVY); but even a difference so slight as to be almost impossible to detect chemically might be sufficient to account for a complete conversion of the glycogen of the liver into sugar if the rapid circulation of the blood is taken into account as well as its large volume (FLÜGGE).

The conversion of glycogen into sugar takes place more rapidly when the circulation through the liver is accelerated; and this undoubtedly occurs in certain lesions of the nervous system (BERNARD, CYON), in which the vasomotor centre in the medulla is destroyed, or the vasomotor nerves of the hepatic vessels divided in any part of their course, so as to increase the circulation in the liver.

Such a conversion of the glycogen, however, is said not to occur during life under normal conditions, it even being affirmed that instead the glycogen becomes a source of fat, being merely a preliminary step in the metamorphosis of sugar into fats (PAVY)—an hypothesis that may be probable, but which cannot be regarded as well founded.

McDONNEL is of opinion that the glycogen unites with the nitrogen set free by the disassimilation of fibrin and albumen, so as to constitute a protein compound resembling casein.

Conversion of Glycogen into Sugar.—This, as we have just seen, is what normally occurs in the body under the influence of certain ferments found in the liver as well as elsewhere in the organism, the change being proportioned to the wants of the economy. It has been abundantly proved, for example, that the liver contains an active ferment capable of effecting this conversion. Experimentally it can be shown that the change is readily produced, the presence even of traces of soluble albumen being capable of bringing it about, though the process is very much slower than under the influence of the diastatic ferments contained in saliva or pancreatic juice (SEEGEN). A pure glycerin solution of glycogen apparently only requires the addition of water to render it capable of fermentation. But it would appear that the product of the action of the animal diastase is a mixture of achroodextrin and maltose, only very little dextrose being formed (MUSCULUS and MERING).

Experiments.

I. *To Demonstrate the Presence of Sugar in the Liver.* (The presence of glycogen has already been demonstrated in its preparation).—Feed a large rabbit, and when it is in full digestion decapitate it; then, having opened its abdomen, look for the portal vein, and tie a glass cannula in it. The liver is next to be gently removed, taking great care not to tear it, and to be placed in a large, deep porcelain dish. (The experiment may likewise be performed, and even more advantageously, without removing the liver at all.) Another glass cannula is now fixed in the hepatic vein, and the cannula in the portal vein connected with a pressure bottle. In making the connection care must be taken to exclude air by filling the cannula from the bottom by means of a long capillary pipette. Now turn on a pressure of 2 to 3 inches of mercury, and wash out the liver, collecting at intervals a portion of the washings as they pass through the cannula in the hepatic vein in a series of small beakers that are to be labelled 1, 2, 3, 4, etc. Test each of these for grape sugar with Fehling's solution, but it is generally advisable first to separate the albumen present by boiling after the addition of a drop or two of acetic acid. Sugar will be found in a diminishing quantity in each of the specimens, until its presence can no longer be detected. When all the sugar has thus been washed out, lay the liver aside for some time, and then repeat the process: sugar will again be found. This sugar, according to SEEGEN, is true grape sugar, while that formed by the action of the salivary and pancreatic ferments on glycogen is not true grape sugar, but an allied form.

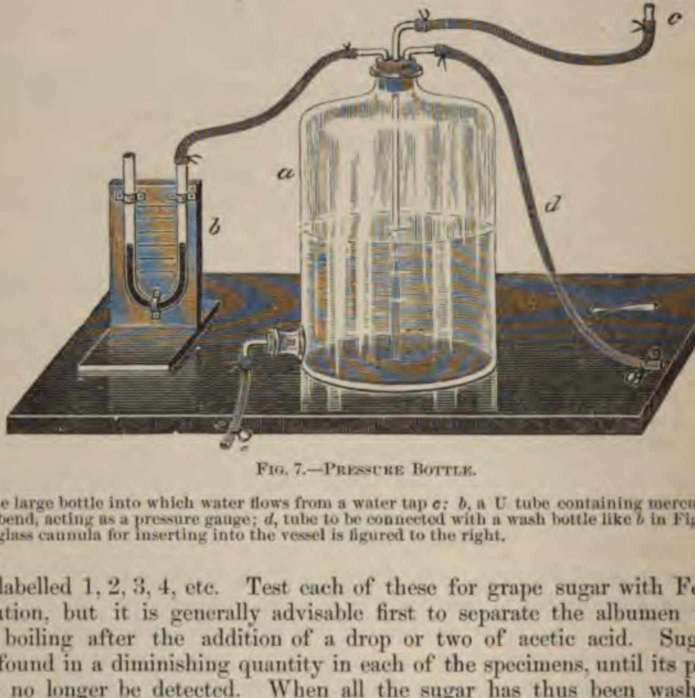


FIG. 7.—PRESSURE BOTTLE.

a, the large bottle into which water flows from a water tap *c*; *b*, a U tube containing mercury in its bend, acting as a pressure gauge; *d*, tube to be connected with a wash bottle like *b* in Fig. 8. The glass cannula for inserting into the vessel is figured to the right.

The *pressure bottle* is easily constructed as follows: Take a very large bottle and stop it with a good cork. In this cork bore three holes, one for a glass tube that will reach to the bottom of the bottle, and which is to be connected by its upper end by means of an india rubber tube with one of the pipes of a water supply or tank, such as are to be had in every laboratory; the second, for a short tube to be connected with a U tube containing some mercury and fixed on a stand; and the third, for another short tube just passing through the cork, its upper end having attached to it a piece of rubber tubing. This last is to connect the pressure bottle with an ordinary wash bottle.

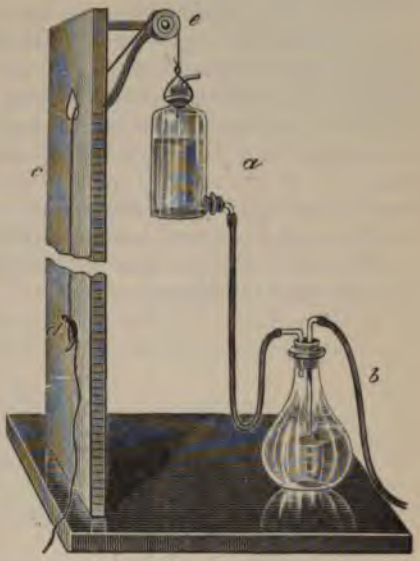


Fig. 8.—Pressure Bottle.

a contains water and is suspended by a cord that passes over the pulley *e*, and is fastened at *d*; *b* is the pressure wash bottle; *c* is the vertical support for the pulley; its front edge is graduated in inches.

To obtain the pressure the plan may also be adopted of suspending a large bottle filled with water over a pulley. In an aperture near the bottom of this bottle is fixed one end of a long piece of flexible tubing, the other end being connected with the pressure bottle. This suspended bottle can be raised or lowered as required by means of the cord attached to it, and if a graduated scale is placed beside it the degree of pressure can be read therefrom, and the U mercury tube rendered unnecessary.

II. *To Prepare the Ferment.*—Place a large piece of the above liver, or better, of a liver just removed, which has been minced and washed in water to remove the blood, in some strong spirit for a few minutes; then remove it, and having dried it, cut it up into very small fragments, that are to be immersed in absolute alcohol and laid aside for 48 hours. When the alcohol has been filtered off, and the mass well washed in more of the same, place it under strong glycerin for a week. The glycerin extract is then to be filtered through muslin.

A similar ferment can be prepared from bile by treating it with alcohol and extracting with glycerin as above.

III. *Tests and Reactions.*—1. Test with a *solution of iodine* made by placing a little fragment of this body in water, and then adding finely powdered potassic iodide with constant stirring until a wine-red solution is obtained; fresh glycogen solutions give a deep vinous red, and the dry powder a chestnut-brown tint. The color disappears on heating the solution, but returns on cooling. Dextrin gives a somewhat similar reaction, but the color does not reappear when the liquid cools.

2. Add caustic potash and a drop or two of cupric sulphate solution: a blue solution is obtained, but on boiling no reduction of the cupric oxide occurs.

3. Boil a little glycogen solution with a few drops of dilute hydrochloric acid: sugar is formed, which can be detected, after neutralization with caustic potash, by boiling with a little Fehling's solution, when a yellowish precipitate is obtained.

4. Add to the glycogen solution some glycerin extract of liver ferment, and warm for a short time to 45°–50°: sugar is rapidly formed, which can be detected as in the previous test. The presence of free

acids, alkalies, alkaline carbonates, or sodic silicate interferes with the conversion.

The glycerin extract acts equally well with starch mucilage, but if the extract is boiled its ferment action is destroyed.

5. Place some glycogen solution in three test tubes, and add to one of them a little blood, and to another a little saliva; lay the three tubes aside for about twenty minutes at a temperature of 37°, and then test them for sugar: this will be found in the tubes to which the blood and saliva have been added, but not in the third. A ferment must, therefore, be present in the blood and the saliva of the same nature as that contained in the glycerin extract of the coagulated liver.

6. A watery solution is precipitated by plumbic acetate, thus differing from dextrin, but, as with dextrin, a precipitate is thrown down by plumbic acetate and ammonia.

CHAPTER XI.

CANE SUGAR, LACTOSE, AND MALTOSE.

CANE SUGAR, $C_{12}H_{22}O_{11}$, is generally distributed throughout the vegetable kingdom in the juices of plants, trees, and fruits.

It forms transparent, colorless, rhomboidal prisms that are very soluble in water, the solution polarizing to the right (73·8°). In its decompositions it resembles grape sugar and it forms combinations with many alkaline and earthy salts.

Though closely allied to grape sugar there are many points of distinction: thus it is not directly fermentable, being first resolved, under the influence of yeast at a warm temperature, into dextrose and lævulose, which then enter into fermentation. When boiled with dilute acids it is likewise resolved into these two bodies. Cane sugar does not reduce Fehling's solution, nor is it precipitated by basic acetate of lead, although it is precipitated by ammonic lead acetate. Strong sulphuric acid chars cane, while it dissolves grape sugar.

Before cane sugar leaves the alimentary canal by absorption it most probably first undergoes conversion into grape sugar. This conversion is generally completed before it passes the ileum, much cane sugar being found in the upper part of the small intestine (KÖBNER). When it is injected into the veins of an animal it is excreted in the urine without alteration, which is not the case with grape sugar, and accordingly cane sugar is not directly assimilable, but must undergo a previous conversion into grape sugar.

LACTOSE, or SUGAR OF MILK, $C_{12}H_{22}O_{11}+H_2O$.—How this body is formed, whether from grape sugar or by a decomposition of albuminous bodies in the organism, is still doubtful. It is found, with any degree of certainty, only in milk, although it has been described as occurring in the urine of women in the early days of lactation and after "weaning."

Properties.—Lactose closely resembles cane sugar, but it is a more stable body. It crystallizes in right rhombic four-sided prisms that are hard and white or nearly colorless, but it is not so soluble as the other sugars; thus it dissolves in six parts cold and two and a half parts hot water, and is insoluble in absolute alcohol and ether, and has only a faint sweet taste. Like dextrose its freshly prepared solution has a dextro-rotary power (93·1°), that diminishes slightly on standing, its warm watery solution polarizing to the right 58·2°, rising to 59·2° when boiled; but it is more or less constant at 52·5°, independent of the strength of its solution.

It is fermentable with difficulty, first, however, being changed into galactose, an isomer of glucose. When it decomposes in presence of casein it forms lactic and sometimes also butyric acid. This can be shown by adding oxide of zinc and casein to its watery solution, and keeping the mixture some time between 35° and 40°: lactate of zinc is formed. Its compounds with bases are unstable, being decomposed readily by boiling.

Acted on with nitric acid it yields mucic and saccharic ($C_6H_{10}O_8$), oxalic, carbonic, and tartaric acids. It is precipitated by basic acetate of lead and ammonia, and reduces alkaline cupric solutions, but less powerfully than glucose (about seven-tenths); so also with the other reduction tests (see under Grape Sugar), such as those of bismuth, silver, and indigo.

Preparation.—1. Add to cow's milk one-fifth its weight of powdered plaster of Paris; boil and evaporate to dryness; exhaust the dry residue with ether to remove fatty matter, and then treat with spirit to remove the sugar present, from which it is obtained by crystallization.

2. Boil the milk and then add a few drops of acetic or hydrochloric acid, so as to separate the curd; filter through linen, and clarify the whey when cold by mixing with it a little well-beaten white of egg and then boiling the mixture; filter again through linen or muslin, and evaporate the filtrate to a syrupy state; lay aside in a cool place for a few days, and purify the crystalline mass obtained by boiling it with animal charcoal; then recrystallize.

3. Acidulate so as to precipitate the casein, filter through linen, boil the filtrate, and filter again; evaporate finally to a small bulk, and lay aside to crystallize.

To Detect Sugar in Milk.—Acidulate slightly with acetic acid, boil, and filter, and test the filtrate with Fehling's solution and with bismuthic nitrate solution (see under Grape Sugar).

MALTOSE is the end product of the action of diastase on starch, and can also be formed by the action of dilute sulphuric acid on the same body. It resembles cane sugar in many respects, but, unlike it, maltose possesses the power of reducing an alkaline solution of cupric hydrate, its reducing action, however, being about one-third less than that of dextrose, but it has a stronger dextro-rotatory power than this body (150°), and, like it, is capable of undergoing alcoholic fermentation; it can also be converted into dextrose by being warmed for some time with a dilute acid. It is said to form fine acicular crystals. Under Digestion reference will be made to the probability of this body being the chief sugar formed by the action of the animal diastase on ferments.

ARABIN is the main constituent of gum arabic. When heated with dilute sulphuric acid it yields a crystalline sugar, *arabinose*, that is isomeric with dextrose, like this body reducing an alkaline solution of cupric hydrate and polarizing to the right, but more powerfully; unlike, however, in being incapable of fermentation with yeast.

CHAPTER XII.

GRAPE SUGAR.

GRAPE SUGAR (*Dextrose*), $C_6H_{12}O_6+H_2O=\left.\begin{array}{lcr}C & \ldots & 36\cdot36\\ H & \ldots & 7\cdot07\\ O & \ldots & 56\cdot57\end{array}\right\}$: $C_6H_{12}O_6=\left.\begin{array}{lcr}C & \ldots & 40\cdot0\\ H & \ldots & 6\cdot6\\ O & \ldots & 53\cdot34\end{array}\right\}$.—Its rational formula may be written $C_5(OCH)H_6(OH)_5$ or $CH_2OH(CHOH)_4COH$. In some respects, we have seen, it corresponds to an alcohol, and in others to an aldehyd.

This sugar is found in the chyle after the ingestion of starchy or saccharine food, in the blood, especially of the hepatic vein, in the lymph, muscle juice, and in the intestinal contents. According to BERNARD in the blood of the carotid of dogs it forms 0·110 to 0·151 per cent., and in that of the jugular 0·067 to 0·125 per cent. In the blood of the carotid ABELES found 0·049 per cent., and in the venous blood of the right heart 0·054 per cent. The estimates given by different experimenters of the comparative amounts of sugar in the blood of the portal and hepatic veins vary considerably, some corresponding more or less with BERNARD'S results, and others differing therefrom. So also with regard to the proportion of sugar in the blood of the right and left heart, but careful experiments point to the proportion of sugar in the right heart exceeding that in the left (LUSK, etc.)

Properties.—Pure glucose does not crystallize well, sometimes appearing as little warty masses, or as little clusters of fine needles, or of radiating rhomboidal lamellæ, or in six-sided tables or prisms, occasionally also in cubes or square tables. The crystalline modification passes readily into the amorphous form when its solutions are boiled or allowed to stand for some time. From hot absolute alcohol it crystallizes in white anhydrous needles that are closely packed in little warty masses. It is not so sweet as cane sugar, easily soluble in water, but less so than cane sugar, very slightly soluble in alcohol, and insoluble in ether. Its watery solutions polarize strongly to the right: 53·1° (TOLLENS), or the crystalline form 56·4°, and the amorphous 56° (HOPPE SEYLER). Freshly prepared watery solutions may indicate 104°, but on heating the solution, or after it has stood some time, it falls to 56°, where it remains constant.

An alkaline solution forms a deep blue fluid with cupric salts, which is decomposed by boiling, the cuprous oxide being precipitated; but this reaction is hindered somewhat by the presence of albumen, peptones, pepsin, kreatin, and kreatinin.

Preparation. (*a*) *From Cane Sugar.*—Add 30 c.c. strong hydrochloric acid to 500 c.c. alcohol (80 per cent.), and saturate the mixture with finely-powdered cane sugar. After standing some time grape sugar separates in a chemically pure form in white crystalline crusts. Collect the crystals by decantation, and after washing them upon a filter with absolute alcohol until the acid reaction disappears dry them in a warm chamber, and lastly recrystallize them from boiling absolute alcohol.

By this process grape sugar is obtained with less trouble and expense than by the following method.

(*b*) *From Diabetic Urine.*—Evaporate the urine at a low temperature to a syrupy consistence, and at the end of a few days or weeks an abundant crystallization appears. Decant and rub up the saccharine mass with a little alcohol, treat it with more spirit, and decant again; then boil with still more alcohol, filter, and allow the filtrate to crystallize. By repeated crystallizations from alcohol the sugar can be obtained free from color and in the form of four-sided prisms, sometimes united in warty masses.

(*c*) *From Starch.*—Boil the following mixture for 4 or 5 hours: potato starch 15, sulphuric acid 6, water 60. Then neutralize with chalk, filter, and evaporate the filtrate rapidly to a small bulk, from which much of the color may be removed by shaking it up with animal charcoal. The ultimate filtrate is evaporated to a thin syrup and allowed to crystallize out.

(*d*) *From Honey*, of which it forms the solid crystalline portion, it may be readily prepared by washing away the fluid syrup with cold alcohol.

Combinations.—It combines with certain acids and bases (as potash and lime), forming glycosates or saccharates; when, for example, an alcoholic solution of glucose is mixed with an alcoholic solution of caustic potash, the saccharate ($C_6H_{11}KO_6$) separates after some time, but its watery solutions give no precipitates with earthy or metallic salts; only in presence of ammonia is it thrown down by neutral or basic acetate of lead, by which, however, it is then readily and completely precipitated. From a concentrated solution of grape sugar saturated with sodic chloride large rhombohedric or double pyramidal crystals, having the composition $2C_6H_{12}O_6+NaCl+H_2O$, often separate on allowing the solution to evaporate spontaneously.

Decompositions.—If 1 molecule of grape sugar is mixed with 5 molecules of cupric sulphate and 11 molecules of sodic hydrate, and the mixture laid aside for 20 minutes, the copper will be precipitated completely, and the filtrate will be free from sugar (SALKOWSKI). In alkaline solutions it has therefore a great tendency to absorb oxygen, and accordingly acts as a strong reducing agent. Most of its tests really depend on this property.

When boiled with the stronger acids and alkalies grape sugar is decomposed; with nitric acid it forms saccharic and oxalic acids, and with dilute sulphuric or hydrochloric acids it is converted into brown substances—ulmin, ulmic acid, etc.

Under the influence of yeast it ferments at a temperature from 10° to 40°, but best at 25° to 35° (below 5° or above 45° fermentation completely ceases)—$C_6H_{12}O_6=2(C_2H_6O)$ (alcohol) $+2CO_2$, a little amyl alcohol, glycerin, and succinic acid being formed at the same time. A complete fermentation will not occur if the percentage of sugar is much above 15 per cent., an accumulation of alcohol also hindering the process.

Grape sugar is readily convertible into lactic and even butyric acid in presence of organic bodies in a state of change, such as are to be found, for example, in the alimentary canal. By mixing with some dextrose a little cheese, decaying albumen, or sour milk, lactic and then butyric acid fermentation will be set up, with the evolution of carbonic acid and hydrogen.

When heated glucose melts, water is given off, and glucosan formed; at a higher temperature more watery vapor is evolved, and at about 170° it is changed into caramel.

Origin, Rôle, and Destination.—The sugar in the body is derived partly from the sugar and starch contained in the food, but a part is undoubtedly formed in the organism itself, particularly in the liver and in muscle, and very probably from the glycogen.

Its rôle is chiefly that of a respiratory food, its combustion into carbonic acid and water giving out much heat; but whether these products are direct or not it would be difficult to say; that there are intermediate products, however, is very likely, as is evidenced by the occasional presence of aceton in the urine, especially of diabetes, and occasionally in the urine of fevers (variola, typhus, pneumonia). MIALHE was of opinion that the sugar, when it arrived in the blood, formed glycosates that were rapidly transformed, ultimately undergoing oxidation. It is probable also that it aids in the development of muscular energy.

Tests.—Before trying *Trommer's test* it is generally advisable for the student to refresh his knowledge of some of the chemical properties of sulphate of copper, and accordingly apply the following tests to a solution of that body: (j) Add *caustic potash*—a light blue precipitate of the hydrated oxide, insoluble in excess. Boil, and the blue hydrated oxide is decomposed, the black oxide being deposited. (ij) Repeat the experiment, but first add some potassic tartrate; the blue precipitate is now soluble in excess, a clear blue fluid being obtained, on boiling which no precipitate is thrown down. (iij) Next substitute glycerin for the potassic tartrate, and note that the same result is produced as before. (iv) The same experiment is to be again repeated, but this time after the addition of sugar, when it is to be observed that the precipitate is soluble in excess of caustic potash, but also that on boiling the suboxide is thrown down, owing to a reduction of the cupric salt. (v) Perform the last experiment again, and note the influence exerted by the addition of ammonia or its salts (the chloride, urate, etc.) in preventing the reduction; then boil for some time with excess of caustic potash, and after the consequent evolution of ammonia it will be found that the suboxide will generally be obtained (BEALE).

1. *Trommer's Test.*—Add a drop or two of a *dilute solution of cupric sulphate* to the solution of sugar, so as to give the mixture a very pale blue tint; now add caustic potash or soda in excess: a pale blue precipitate of cupric hydrate is thrown down, which immediately redissolves, a deep blue solution being formed. Heat gently, and generally before

the boiling point is reached a *reddish, orange, or yellow precipitate* of the suboxide of copper will show itself, appearing first near the surface of the liquid. The color of the precipitate depends on the relative proportions of the sugar and copper, with excess of sugar being yellowish and with excess of copper reddish; but this is also affected greatly by the degree of concentration and the purity of the solutions employed, with impure solutions, as with urine containing little sugar, the suboxide having generally a yellow color.

It is much safer to employ a little Fehling's solution in applying this test, as many liabilities to error are thus avoided. Place some of the solution in a test tube, dilute it with water, and boil; then add the saccharine fluid drop by drop and continue the application of the heat: a yellow or red sediment will soon form before boiling point is reached. The plan of boiling the urine first and then adding the reagent is not to be adopted.

If albumen is present, as occasionally happens with saccharine urine, it is advisable to separate this body before applying Trommer's test. This is readily done by acidifying the liquid with a drop or two of acetic acid, then boiling for some time, filtering, and washing the precipitated albumen on a filter.

2. *Moore's Test.*—To a little of the solution add *half its volume of liquor potassæ* and boil gently for a minute or two: a bright brown tint is acquired by the fluid. The change in color will be better seen if only the upper part of the mixed liquids is heated. It is due to the formation of melassic acid, and if a little nitric acid in excess is next added, an odor like that of burnt sugar or of formic acid will be evolved.

The test is wanting in delicacy. Care should be taken that the caustic potash contains no trace of lead.

3. *Reduction Tests.* (*a*) *Maumené's.*—When glucose is heated in contact with *perchloride of tin* ($SnCl_4$) decomposition occurs and a black compound is formed.

The test may be conveniently applied thus: Dissolve some of the perchloride in twice its weight of water and filter; immerse long strips of any woolen material, such as white merino or flannel, in this solution, and then dry them over a water bath at a gentle heat; these strips are to be kept in a bottle till required. Dip one of them in a very dilute solution of the grape sugar, and heat the moistened slip before a fire, or otherwise (at a temperature of 130° to 150°), and it will quickly assume a brownish black color.

Other carbohydrates, however, possess the same property.

(*b*) *Böttger's Bismuth Test.*—This may be performed in any of the three ways given below; the third, however, is to be preferred; but no albumen must be present.

(j) Add a few drops of dilute nitric acid solution of nitrate of bismuth to the solution of sugar, then render the mixture alkaline by the addition of sodic carbonate and boil a few minutes; the bismuth salt is reduced and a *gray or black precipitate* is thrown down.

(ij) Boil some of the grape sugar solution and saturate it with sodic carbonate in substance, then add a few grains of basic bismuthic nitrate and boil a few minutes; a gray and then a black precipitate of metallic bismuth soon appears.

(iij) First prepare an alkaline solution of the oxide of bismuth: take 5 grams basic nitrate of bismuth and 5 grams powdered tartaric acid, and place in a small flask with 30 c.c. distilled water; now add slowly and with constant stirring some strong solution of caustic soda until a clear solution is obtained. Close the flask with a caoutchouc stopper through which passes a tube filled with fragments of caustic lime.

Add a little of this to the solution of sugar and boil for a few minutes, when a marked brown and then a black coloration shows itself, a black powder subsequently separating.

(c) *Silver Test.*—Add ammonia in excess to a little strong solution of silver nitrate, then boil after the addition of the grape sugar; the silver salt will be reduced and form a mirror in the bottom of the tube.

Aldehyde and tartaric acid, however, give the same reaction.

(d) *Indigo Carmin.*—Add some sodic or potassic carbonate to a dilute grape-sugar solution, and then sufficient solution of indigo carmin to impart a blue coloration; boil, and a *yellow color* will ultimately make its appearance, indigo white being formed, the blue changing to green and then to reddish purple and red. The blue tint may be restored by pouring the fluid into a small flask and shaking in the air for some time, but the yellow color soon reappears.

4. *Picric Acid Test.*—Mix with the sugar solution an equal volume of a saturated solution of picric acid, and heat the mixture gently after the addition of a few drops of liquor potassæ; a *deep red brown color* gradually appears.

5. *Fermentation Test.*—This is one of the most satisfactory tests for sugar, but it fails if only slight traces (below 0·5 per cent.) are present.

(a) Fill a large test tube with a dilute solution of the sugar, and after adding a little dried German yeast, or some fresh yeast, invert the tube over some more of the same solution of sugar, or better over a layer of mercury in a small evaporating dish, closing the mouth of the tube with the finger or with a pad of india rubber in doing so. Lay the whole aside in a warm place (about 25°) for 24 hours. The sugar will undergo fermentation, alcohol and carbonic anhydride being formed, the latter accumulating in the test tube and displacing the fluid. *To identify the carbonic acid* gas, close the lower end of the inverted tube with the thumb, and transfer it to a dish containing water; then fill a small test tube with water, and having inverted it in the same dish, bring the mouth of the largest test tube under that of the small one, so as to allow a little of the gas to escape and enter it. Test the carbonic acid gas thus obtained by the addition of clear lime water, which at once becomes milky on shaking it with the gas from the formation of carbonate; or by passing a piece of solid caustic potash into it when over mercury, by which means the gas will be absorbed.

As the yeast itself, from being impure, frequently evolves carbonic acid, as a precaution place the same quantity of yeast in another test tube filled with water, and proceed with it as with the solution of sugar.

(b) When only a small amount of sugar is present, say in urine, the test may be thus applied: The dilute saccharine solution is acidified with a drop of acetic acid and a small piece of yeast well mixed up with it; it is then transferred to the cylinder *a* in the adjoining apparatus, so as to fill it, and then into the narrow part of the cylinder *b* some mercury is poured. The whole is set aside in a moderately warm place (30°).

In a few hours gas is disengaged and collects in the upper part of *a*. To prove it to be carbonic acid fill the wide part of the cylinder *c* with caustic potash; then having closed the orifice with the finger, shake vigorously, when the gas will be absorbed. It is advisable to make a control experiment at the same time, replacing the saccharine solution or urine with water.

To render the experiment conclusive by *detecting the presence of alcohol*, which, however, is unnecessary, the dilute saccharine solution should be evaporated to half its volume before adding the yeast, and the fermented fluid afterwards treated with benzoyl chloride, which causes benzoic ether to be evolved (BERTHELOT). Or distil and mix the distillate with a little solution of iodine in potassic iodide; add caustic potash drop by drop till the color disappears, when it is to be laid aside for some time: a yellowish color appears and a sediment soon forms, showing six-sided crystalline tables of iodoform under the the microscope.

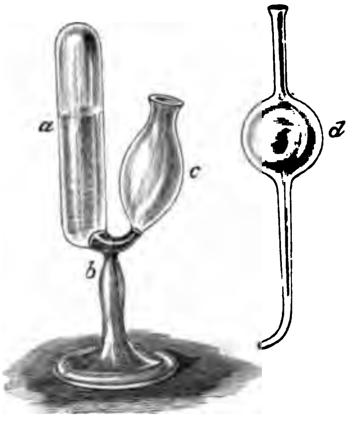


FIG. 9.—APPARATUS FOR SUGAR FERMENTATION TEST.

This is to be recommended when the amount of sugar present, as well as of the urine or other fluid containing it, is small. *a*, cylinder into which the fluid is to be passed by means of *d*, the whole vessel being inclined, and in which the carbonic acid gas accumulates; *b*, a little quicksilver at the narrow communication between *a* and *c*, acting as a valve, and allowing the escape of the fluid from *a* to *c* as the gas is generated.

(*c*) Two little flasks connected together, as in Fig. 13, can also be used. One (A) is half filled with the saccharine fluid, 2 or 3 drops strong solution of tartaric acid added and then a piece of yeast. The gas when generated, passes into the other flask (B), which is half filled with baryta water, by which it is absorbed and baric carbonate formed. Lay the apparatus aside at a temperature of 20° to 25°.

(*d*) Fill a long test tube with solution of sugar and the yeast, and through the cork closing its mouth pass a narrow glass tube to the bottom of the test tube. Attached to the outer end of the narrow glass tube is a piece of india rubber tubing, which dips into a small flask. Place the whole in a warm chamber at 35°. The carbonic acid generated will drive out the fluid into the flask, where it can be tested for alcohol by one of the delicate methods given under *b*, or by boiling it with a little potassic bichromate and sulphuric acid, when a green coloration is produced.

The Yeast Growth.—During the process of fermentation the yeast grows at the expense of the sugar, and a characteristic delicate white scum accumulates on the surface of the liquid, which on microscopic examination will be seen to consist of torula stems, and great numbers of minute oval vesicles. These granules, or *torulæ*, are single or associated in clumps, or united end to end. Each granule is round or oval and transparent, having an average diameter of $\frac{1}{3000}$ of an inch, and consisting of a little thin-walled cell filled with a semi-fluid matter or protoplasm in which a clear space or vacuole is generally to be seen. The torulæ are living bodies that under favorable conditions grow and multiply, chiefly by a process of budding, and as the result of their vitality the series of fermentation products are manufactured by them from the food substances contained in the fluid in which they float. The presence of nitrogen, phosphorus, sulphur, potassium, and magnesium in some of their combinations appears to be necessary to their growth, their development being an essential part of the fermentation process, the cells living and growing at the expense of the sugar, causing it to break up into simple substances by withdrawing from it a portion of the material necessary for their continued sustenance. Some of the by-products of the fermentation are possibly not formed by the splitting up of the sugar, but are the result of some secondary action, water probably being at the same time decomposed into its elements and nascent hydrogen playing an active part.

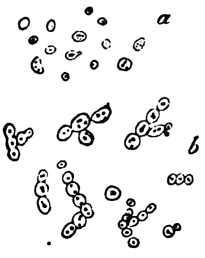


FIG. 10.—YEAST TORULÆ. *a*, at rest; *b*, in different stages of activity.

Influence of Acids on the Formation and Activity of Yeast.—So far as acids are concerned, fermentation is aided by the presence of sulphuric acid 0·02 per cent. and of lactic acid 0·1 to 0·2 per cent., while it is retarded by the presence of sulphuric acid 0·2 per cent., hydrochloric acid 0·1 per cent., phosphoric acid 0·4 to 0·5 per cent., and lactic acid 2·5 per cent. Fermentation is suppressed by sulphuric acid when present in the proportion of 0·7 per cent., hydrochloric acid 0·5 per cent., phosphoric acid 1·3 per cent., and lactic acid 4·6 per cent. (HAYDUCK).

6. *The presence of sugar in normal urine*, in which it exists in very small amount, may often be shown by the following modification of *Brücke's method:* 200 to 300 c.c. fresh urine are treated with excess of boiling saturated solution of chloride of lead, filtered, and the filtrate precipitated with ammonia; the precipitate is collected, washed, suspended in water, and decomposed with sulphuretted hydrogen. It is again filtered, and the filtrate, when boiled to separate the excess of hydric sulphide, will give with Fehling's solution an abundant deposit of the cuprous oxide.

7. *Precipitation by Potash and Alcohol.*—By this process very dilute solutions of sugar can be tested. To a little of the dilute solution of grape sugar add 4 times its volume of absolute alcohol, filter after it has stood aside for several hours, and pour into the filtrate a little alcoholic (80 per cent.) solution of potash; now set aside for a couple of days, when a deposit consisting of a combination of the potash and grape sugar occurs on the sides of the vessel. Drain off the liquid, dissolve the deposit in a little water, and test the solution by any of the usual reagents; or the watery solution of the deposit may be neutralized with acetic acid, precipitated with acetate of lead,

filtered, the lead separated by means of hydric sulphide, and the filtrate, which serves for the sugar tests, partially evaporated.

8. In the case of blood, chyle, etc., evaporate the serum to dryness and exhaust the residue with spirit: evaporate this to dryness, and exhaust the residue again with the spirit, which is in turn to be evaporated to dryness and its residue dissolved in water. With other fluids, or watery extracts of organs, first exhaust with spirit, evaporate the spirituous extract, dissolve the residue in water, add to this watery extract 2 or 3 drops of acetic acid, and evaporate again; dissolve this last residue in water and apply the copper test.

CHAPTER XIII.

QUANTITATIVE DETERMINATION OF GRAPE SUGAR.

The amount of sugar present in a solution can be determined: (1) by the polariscope, (2) by Fehling's solution, (3) by standard cyanide of silver solution (KNAPP), (4) by standard silver iodide solution (SACHSSE), (5) by the amount of carbonic acid gas produced in the fermentation of a given quantity, and (6) by the alteration in the specific gravity effected by fermentation (ROBERTS).

I. By Polarization.—Before describing the process it may be advisable to explain the principle upon which it is founded. When a ray of common light passes through certain crystals it is split into two rays, one of which undergoes ordinary refraction; the other takes a new or extraordinary course, and is said to be polarized. Certain doubly refracting crystals like tourmaline tend to absord one of these rays (the *ordinary*) and let the *extraordinary* ray pass. If two similar plates of tourmaline are held with their axes parallel light passes through both, but if they are turned with their axes at right angles the light is almost entirely stopped, the light that has been polarized by passing through the first plate not being able to make its way though the second. Nicol's prisms, consisting of specially cut and conjoined prisms of Iceland spar, act like the tourmaline, allowing the polarized light to pass through both prisms except when they are crossed. With the polarizer and analyzer, as these prisms are named, so arranged as to allow the light to pass, a certain degree of color will be observed, which changes in tint as the analyzer is rotated. If now there be placed between the two prisms thus crossed, so as to stop the light, a plate of rock crystal cut at right angles to the principal axis, it will be found that the light passes, so that the rock crystal must have caused a certain degree of circular rotation of the polarized ray in its passage through before it arrived at the second prism or analyzer; indeed, its passage through the latter prism can be interrupted by turning this prism round to a certain extent, the amount of rotation required depending on the thickness of the rock crystal and on the color of the light employed, less rotation being required with red than with the other primary colors towards the violet end of the spectrum. With some

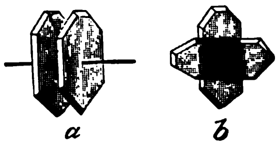


FIG. 11.—TOURMALINE PLATES.

a, prisms placed one behind the other with their long axes parallel (light polarized by the first goes through the second unaltered); *b*. prisms crossed at right angles (the light polarized by the first plate is stopped by the second, and complete darkness ensues).

plates the rotation is towards the right-hand, and with others towards the left. This kind of polarization is therefore called circular, the expression ***rotation towards the right*** being applied to a movement in the direction of the hands of a watch as seen by the observer, and rotation in the opposite direction termed ***left-handed.***

Solutions of many organic bodies, such as cane and grape sugar and tartaric acid, etc., exhibit a right-handed rotation, and accordingly are said to be *dextro-rotatory;* while others, like a solution of albumen, or uncrystallized sugar, and spirits of turpentine, rotate the light towards the left and are accordingly named *lævo-rotatory.*

Suppose now the two prisms are so arranged as to extinguish the light completely, and a tube filled with a solution of grape sugar is interposed between them; it will be found that the solution acts like the rock salt in partially restoring the light. On rotating the analyzer, or prism near the observer's eye, through a certain angle the light is again extinguished, and it will be seen that the amount of rotation required is jointly proportional to the length of the tube holding the sugar and to the strength of the solution.

As the amount of circular polarization varies with the body as well as with the strength of its solution, the method can be employed in determining the strength of such solutions, as in the case of the saccharimeter used for saccharine solutions.

There are different forms of this instrument, but they correspond in having two Nicol's prisms so arranged as to leave a space between to receive the tube for the solution of sugar, the prism through which the light passes before entering the solution being named the polarizer, and the other the analyzer, as it requires the one to produce the polarization and the other to show it. The prisms are first crossed so as to stop the light; the tube with the sugar is then inserted, when it will be noticed, as above explained, that the light is enabled to pass. It is then necessary to rotate one of the prisms through a certain angle before the light is again excluded, and this angle is measured on a circular graduated disk, the prism in being rotated, carrying an index with it, which moves along the divisions on the disk. The difficulty lies in determining when the field of vision is darkest, and several additions have been made to render this more accurate.

The adjoining diagram will illustrate the different parts of the saccharimeter, as well as the additions referred to.

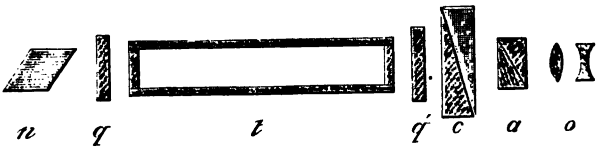


FIG. 12.—DIAGRAM OF A SACCHARIMETER.

n is the Nicol's prism, or polarizer, upon which the light falls.

q is a layer of quartz, composed of two halves of equal thickness, one dextro- and the other lævo-rotatory, their line of junction being in the axis of the instrument.

t is a brass tube closed at its extremities with glass, to be filled with the saccharine solution to be tested.

q' is another plate of quartz, lævo-rotatory.

c, the compensator, consists of two right-angled prisms of dextro-rotatory quartz, which slide one on the other by means of a rack and pinion movement, so that the thickness of the combined plate can be altered, its effect of course increasing in proportion to the overlapping of the plates, and thus compensating more or less the effect produced by the lævo-rotatory quartz plate q'. In their mean position, marked by the zero of the scale, their thickness exactly equals that of the plate q', and accordingly they destroy its lævo-rotatory action.

a is the analyzer.

o is the ocular, consisting of two lenses, that enable the observer to see distinctly the vertical line of separation between the two halves of the double quartz plate.

A scale and vernier are attached to indicate the relative position of the parts of the compensator, the zero of the scale corresponding to an exact compensation of the lævo-rotatory quartz; and accordingly when the screw is moved, so as to increase the thickness of the compensator, a dextro-rotation ensues, the contrary effect being produced by moving the screw in the opposite direction.

When the analyzer is looked through two distinct colors will be seen, corresponding to each of the two halves of the quartz plate q; but by turning the analyzer on its axis the whole field can be made to assume the same tint. If now the tube t is filled with a solution of sugar, it will be found on examination that the previous uniformity of the field has departed, and that a difference of color shows itself, corresponding to the two halves of the plate q. This is due to the sugar, which increases the action of the dextro-rotatory and diminishes that of the lævo-rotatory segment—a difference, however, that can be removed by the rotation of the analyzer a, or more delicately by means of the compensator. From the amount of screwing the compensator requires, which is read off on the scale attached, the percentage of sugar is determined; the $+$ sign prefixed to the number indicates right-handed polarization, and the $-$ sign left-handed.

Different saccharimeters are employed. The above description refers more particularly to the construction of Soleil-Ventzke's instrument. Mitscherlich's is much simpler.

Saccharimetry.—*Process* 1. *If we use a Mitscherlich's instrument* with a double quartz plate (like q in the above diagram), the tube is placed horizontally with the polarizer in front of the aperture in a cylinder surrounding a luminous flame of some kind. The analyzer is then moved until the two halves of the visual field of the double plate offer the same *teinte de passage*, say a reddish violet, which in a good instrument is generally indicated by the index pointing to the zero of the scale; a central vertical black line indicating the crossed position of the Nicols is also visible. First make a solution of the sugar containing one gram to each c.c., and completely fill the tube between the prisms with this solution. Now look through the instrument, and it will be found that the two halves of the visual field are unequally colored. Turn the analyzer to the right or left until the same *teinte de passage* is obtained as before the insertion of the sugar, and note on the scale the number of degrees corresponding to the angle of rotation; this gives the *specific rotation*, by which is meant the rotation effected by a solution of the substance containing one gram in one c.c. of liquid when contained in the one-decimetre tube. With any known strength of solution (which should be concentrated) the specific rotation will be obtained by the following formula for yellow light:—

$s=\frac{a}{wl}$, where s=specific rotation.

a=rotation observed.
w=weight of the substance in grams contained in one c.c. of liquid.
l=the length of the tube.

To find the value of w, the formula is thus modified: $w=\frac{a}{sl}$

In the case of diabetic urine, when we employ a tube one decimetre long, the degrees of the scale give approximately in grams the percentage richness in sugar. With a two-decimetre tube first halve the number of degrees. More exactly the percentage is obtained by the formula $x=\frac{100\times a}{56^\circ}$, where x is the percentage sought, a the rotation with the one-decimetre tube, and 56° the specific rotatory power of grape sugar.

The solution of sugar should be clear, or at least not present more than a slight yellow tint; otherwise the excess of color must be removed by filtration through animal charcoal. It should also be free from polarizing bodies, like albumen, etc.

2. *With Ventzke-Soleil's saccharimeter*, arrange the instrument horizontally before the source of light, cutting off excess as before, and the movable Nicol is turned until the field assumes a pale rose or violet tint. This color serves best for estimating the difference of color in the two halves of the field of vision, and is therefore to be preferred. This done, the eye-piece of the small telescope is to be adjusted so as to enable us to see distinctly the line separating the two halves of the double plate. The rack of the compensator is next to be turned one way or other till we render the two halves of the field perfectly identical in tint. Repeat this operation several times, and then note if at this point it corresponds to the zero of the scale. If not a correction must be made with the little button below the fixed Nicol, by means of which the latter is turned a little to one side or other; but this is rarely required, and should not be attempted by the ordinary student. At the zero of the scale, if the instrument is correct, the dextro-rotatory plates of the compensator are of such thickness and power as exactly to neutralize the lævo-rotatory power of the plate of quartz.

When working with an accurate instrument we may proceed at once to the estimation by making the zero of the vernier coincide with the zero of the upper scale, focussing, and coloring the field of vision of a rosy tint. The instrument is well arranged if the two halves of the field continue of the same color however the movable Nicol is turned. The clear saccharine solution or urine is then carefully poured into one of the tubes for the purpose so as to fill it *completely*, and it is inserted in its place in the polariscope. This tube should be kept very clean, before each determination being washed out with a little of the solution to be tested, and after the experiment with distilled water. Care should be taken to exclude air, and not to screw up the glass plates at the ends of the tube too tightly.

On examination the coloration of the double plate will no longer be seen to be uniform; we therefore turn the rack of the compensator to the right, so as to try to reproduce the two halves of the field with exactly the same tint. The movable Nicol may also be moved, if this has not already been done, so as to secure a rose or other tint in which the observer can most sharply distinguish the least difference of color in the two halves of the double plate; and when we have obtained a uniform coloration, say of a rosy tint, the movable Nicol may be rotated to ascertain if the uniformity of the field persists with the change of color. The observations, it may be remarked, should, for the sake of accuracy in the judgment of minute differences of color by the eye, be made as rapidly as possible, ten seconds at a time being fully sufficient.

The scale of the compensator is then read, and the zero of the vernier will be seen to the right of the zero of the scale, indicating a dextro-rotatory body. The compensator is generally graduated, so that each degree of its scale represents 1 gram of sugar in 100 c.c. of fluid when the one-decimetre tube is used at a temperature of about 17°; that is, each degree corresponds to a percentage.

When the two- or half-decimetre tube is employed, the number of degrees must be divided by the length of the tube.

Briefly, the steps may be thus stated: The lamp is arranged so that the light traverses the axis of the instrument, the tube first being filled with pure water; the ocular is then adjusted so that the field may be seen divided into two equal halves, of the same or different tints separated by a sharply defined black line. If the two halves are of different tints, turn the horizontal screw-head one way or other till they are both alike. The tint most sensitive to the observer's eye may be chosen. The zero of the scale ought to coincide with the black line of the indicator; if not, it must be so adjusted. Fill the tube with the sugar solution and examine; the uniformity of tint of the two halves of the field no longer exists. This is re-established by turning the horizontal button; and the original tint, which the solution has generally caused to disappear, must then be restored by turning the milled head.

We therefore start with an equal or similar coloration of the two halves of the double quartz plate, and we finish with the same, the number of degrees through which the compensator has had to be moved to re-establish this giving the strength of the saccharine solution. The observations are best made in a darkened room.

II. **Fehling's Method by a Standard Copper Solution.**—This is founded on the property possessed by grape sugar of reducing cupric oxide (CuO), when present in alkaline solutions, to the state of cuprous oxide (Cu_2O), and depends on the fact that a definite mixture of cupric sulphate, potassic tartrate, and caustic soda undergoes no change on boiling unless sugar is added. SOXHLET and others, however, have shown that the power of grape sugar to reduce this solution is not constant, but varies somewhat under different conditions.

1 eq. grape sugar ($C_6H_{12}O_6=180$) is capable of reducing the 5 eq. (397) of cupric oxide contained in 5 eq. of crystallized cupric sulphate ($CuSO_4+5H_2O=249{\cdot}5\times5=1247{\cdot}5$). The most convenient strength is one of which 10 c.c. fully reduce 0·05 gram of grape sugar, and therefore contain 0·3464 gram cupric sulphate.

Preparation of the Solutions. Standard Copper Solution.—(*a*) Roughly powder some pure crystallized cupric sulphate, and press it between some folds of dry filter paper; weigh 34·64 grams, and dissolve in moderately warm water, which is then to be diluted up to 500 c.c. with cold water. Preserve in a stoppered flask.

(*b*) Dissolve 173 grams Rochelle salts in pure crystals in caustic soda (sp. gr. 1·34) 100 c.c., and dilute with water to 500 c.c. Preserve in a stoppered bottle. Air must be carefully excluded from both solutions, the tartaric acid, for example, in solution *b* tending to change into racemic acid, which reduces cupric salts.

For use, mix equal volumes of the fluids *a* and *b*; on shaking them together a dark blue fluid is obtained, of which 10 c.c.=0·05 gram sugar.

A ***Mohr's*** burette and a pipette capable of delivering 10 c.c. are required. If the Fehling's solution has been prepared for some time it is advisable to boil a little of it and then lay it aside for half an hour, when, if it gives no precipitate, the solution will serve for the analysis.

Process.—The solution to be tested should not contain much sugar; *indeed, it must not much exceed* 0·5 *per cent.;* accordingly strong solutions, and most diabetic urines, should be diluted before being tested. With diabetic urine of high specific gravity dilute with 10 or 20 times its volume of water. Further, if the solution is of a very dark color, or contains extractives that might interfere with the reaction, it is advisable first to boil and then add a little milk of lime, and when the precipitate has settled to filter through animal charcoal and dilute the washings to a definite volume.

Place the *dilute* saccharine solution in the Mohr's burette, and having transferred 10 c.c. of the Fehling's solution to a deep porcelain dish (or small flask), dilute it with 40 c.c. water. Place the dish over a lamp or Bunsen burner, and arrange the burette a little above it on a stand. Heat the diluted Fehling's solution, and when it is beginning to boil allow the sugar solution to flow into it gradually; the red sub-oxide is thrown down, and the blue color of the solution gets less and less. Boil again and repeat the addition of the sugar solution *till the blue color has disappeared*, which is best observed by tilting the porcelain dish from time to time after the precipitate has been allowed to subside (or, if a flask has been used, by holding it before a window), and causing the fluid to rotate slowly round in the dish or flask. When this point has been reached, to insure accuracy (especially with beginners) a few c.c. of the hot fluid should be filtered through a small thick Swedish filter, the filtrate acidulated with acetic acid, and a drop of potassic ferrocyanide added. If copper is present a brown color or precipitate is formed. In this case more of the sugar solution must be added to the diluted Fehling, and the operation completed.

It is always advisable to make a second experiment, and, guided by the indications of the first, to proceed more rapidly, as the precipitated suboxide tends to reoxidize quickly and redissolve; and if comparatively little of the diluted urine was required, the latter may be diluted with 20 instead of 10 times its volume of water; while on the other hand, if but little sugar is present the dilution should be much less, or even no dilution made at all.

Suppose 12·5 c.c. of the diluted urine reduced 10 c.c. Fehling's solution (=0·05 gram sugar), then the percentage of sugar $=\frac{0{\cdot}05\times 100}{12{\cdot}5}=\frac{5}{12{\cdot}5}=0{\cdot}416$; and, as the saccharine solution or urine has been diluted ten times its volume, $0{\cdot}416\times 10=4{\cdot}16$ per cent.; or if it has been diluted 20 times, then $0{\cdot}416\times 20=8{\cdot}32$ per cent.

The results obtained, according to WORM MÜLLER, and HAGEN, are $\frac{3}{10}$ per cent. too high.

The presence of alcohol, chloral, and benzoate of soda in the urine interferes with the accuracy of the process.

Separation of Albumen.—With milk or albuminous saccharine urine acidulate 100 c.c. or so with acetic or hydrochloric acid, boil for some minutes, filter, wash the precipitate, and make up the filtrate to the original volume.

Before Fehling's process can be applied to the *determination of cane sugar*, this body must first be converted into grape sugar by heating some 40 c.c. of its solution 20 minutes or so with 40 drops of dilute hydrochloric or sulphuric acid (1 : 5), taking care not to char the sugar, and to replace the water that has evaporated; then neutralize with carbonate of soda or lime, filter, and dilute with water.

To convert starch into grape sugar, to enable it to be thus estimated, 1 gram or so of it should be made into a mucilage with 40 c.c. of cold water, and heated with 40 c.c. of one of the above dilute acids; but the boiling requires to be continued 8 to 10 hours before the conversion into grape sugar is completed [$3C_6H_{10}O_5+H_2O=C_6H_{12}O_6+2C_6H_{10}O_5$ (dextrin)].

95 parts of cane sugar or 90 parts of starch represent 100 parts of grape sugar.

III. **Knapp's Method by Mercuric Cyanide** depends on the reduction of an alkaline mercuric cyanide solution by the sugar, metallic mercury being deposited, and 100 parts anhydrous grape sugar being equivalent to 400 parts mercuric cyanide.

Dissolve pure and dry mercuric cyanide 10 grams in water, add caustic soda (sp. gr. 1·14) 100 c.c., and make up to a litre. 40 c.c. correspond to 0·1 gram grape sugar. The solution keeps well, and for this and other reasons its use is advocated by some authorities.

Process.—Boil 40 c.c. in a beaker or small flask, and allow the urine or sugar solution, diluted to about 0·5 per cent., to flow in gradually from a Mohr's burette, as in the previous process, with continued heating. The reduced mercury sinks slowly. To ascertain the end of the reaction remove a drop of the clear fluid from time to time with a capillary tube, and place it on a piece of very fine filter paper; expose this spot on the filter paper first to the vapor of hydrochloric acid and then to that of sulphuretted hydrogen; or it may be exposed to the vapor of ammonic sulphide for half a minute or so by bringing a drop down upon filter paper tied over a small beaker containing some strong ammonic sulphide. So long as excess of unreduced mercuric salt is present the entire spot becomes brown, and as less and less is present only the margin is colored, and finally, when it is all reduced, the spot remains transparent. Only the coloration of the *fresh* spot is to be taken as the indicator.

It is advisable to dilute the mercuric solution, and to add the sugar solution in successive portions; rapidity is also necessary, as the deposited mercury redissolves (MÜLLER and HAGEN).

The results are not more accurate than those obtained by Fehling's process, but the standard solution is easier to prepare and keeps better.

IV. Sachsse's Method.—

Mercuric iodide	18 grams.
Potassic "	35 "
Caustic potash	80 "
Water	to 1,000 c.c.

40 c.c. = 0·15 gram grape sugar.

Proceed as in Knapp's process. The end of the reaction is noted by means of a solution of stannous chloride supersaturated with caustic soda. Some drops of this solution are placed on a small porcelain dish and treated with drops of the mixture; so long as the mercuric salt is present in excess a brown color or a gray precipitate appears.

V. The Fermentation Process.—This, as we have already seen, is applied to the peculiar decomposition that most of the carbohydrates of the composition $C_6H_{12}O_6$ undergo, in dilute aqueous solutions, under the influence of beer yeast. It consists mainly in the resolution of the sugar into ethyl alcohol and carbonic anhydride, about 95 per cent. of the sugar appearing to undergo this change. The fermentation occurs most readily between 20° and 40°, best probably about 35°, ceasing at 0° and being retarded by reduction of pressure. $C_6H_{12}O_6 = 2C_2H_6O + 2CO_2$; that is, 1 molecule grape sugar (180 by weight) gives two molecules carbonic anhydride (88 by weight), or 100 CO_2 = 204·54 sugar. The estimation may be made either from the loss in weight of the apparatus, owing to the evolution of the gas, or to the gain in weight of an absorption tube containing caustic potash connected with the escape pipe.

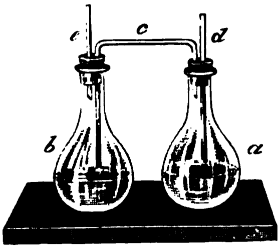


FIG. 13.—APPARATUS FOR ASCERTAINING THE QUANTITY OF CARBONIC ACID FROM THE LOSS IN WEIGHT.

Into *a* is introduced the saccharine solution, together with some drops of a tartaric acid solution, and then a piece of yeast; *b* contains a little strong sulphuric acid, into which the evolved carbonic acid passes through *c* from *a*, and escapes by *e*.

Two small flasks are connected together as in the diagram. Into *a* 20 c.c of the sugar solution or diabetic urine are poured, then some drops of a solution of tartaric acid, and a piece of well-washed yeast added, and *b* half filled with strong sulphuric acid. Now weigh the apparatus and lay it aside in a warm place (20° to 24°), and after 48 hours weigh again, having first heated *a* to about 60°, drawn air through, and allowed the whole to cool. The loss in weight$\times\frac{45}{22}$ or 2·045=the grape sugar.

Experiment.—

	Grams.
Flask and saccharine urine	58·54
Flask	23·32
Urine	35·22
The apparatus before fermentation . .	134·820
The apparatus after fermentation . . .	134·033
Carbonic acid	0·787

As 48·89 CO_2 correspond to 100 sugar, therefore 0·787=1·609 sugar. Accordingly the 35·22 grams of urine contain 1·609 gram sugar, or 1,000 contain 45·68 grams. The same result can be obtained more readily by multiplying the loss in weight by 2·045, as 0·787×2·045=1·609 sugar.

By connecting with the exit tube of *b* a weighed Liebig's bulb apparatus containing caustic potash (sp. gr. 1·27) the dried carbonic anhydride escaping will be absorbed and give rise to an increase in weight. As an additional precaution that the escaping gas should be thoroughly dry before entering the potash bulbs, it may be passed through a drying tube filled with calcic chloride or pumice stone and sulphuric acid.

Each gram or fraction of a gram of increased weight is equal to twice the same amount of sugar, or more correctly to the increase in weight×2·045.

VI. Estimation from Loss of Specific Gravity in Fermentation. *Differential Density Method* (ROBERTS).

Process.—Take *accurately* the specific gravity of the fluid, and in doing so it is better, as Dr. **ROBERTS** advises, to use two urinometers with very long stems, one ranging from 995 to 1,025 and the other from 1,025 to 1,055. The temperature of the liquid should also be taken, and filtration performed if necessary. Place about 4 oz. (0·56 litre) of this fluid in a 12-oz. flask or bottle; add to it a lump of washed yeast the size of a small walnut; then lay it aside, having stopped the mouth with a nicked cork so as to allow the gas to escape. After 24 hours in a warm place allow the scum to subside and take the specific gravity of the decanted liquid. It is often more convenient to place a tightly-corked 4-oz. bottle filled with the same solution or urine, but without any yeast, beside the specimen containing the yeast. After about 18 hours the two bottles can be removed to a cool place for 2 or 3 hours, and their densities then taken. In this way any error as to the effect of difference of temperature on the density can be avoided. The number of degrees of density lost indicates the number of grains of sugar per oz.; and the percentage is obtained by multiplying the degrees of density lost by 0.23. Thus in a urine whose density before fermentation was 1,053, and afterwards 1,004, the degrees of density lost=49, and accordingly 49 grains of sugar are present per oz., or 49×0·23=11·27 per cent.

Manassein gives 0·219 as the multiplier instead of 0·23, and considers that for practical purposes the method may be regarded as very nearly exact. Reckoning, then, each degree of density lost as=0·219 per cent. of sugar, and taking the density to be 1,029 before and 1,005 after fermentation, the difference $24 \times 0{\cdot}219 = 5{\cdot}26$ grams=the percentage of sugar present.

VII. **Vogel** has also proposed a method for the approximative determination, depending on the intensity of coloration produced by boiling the solution to be tested with caustic potash. A standard of comparison is obtained by boiling a definite weight of pure and dry grape sugar with an excess of caustic potash. Dr. **Garrod** uses a strong solution of carbonate of potash instead of the caustic potash. And Dr. **George Johnson** has devised a quantitative method depending on the depth of tint yielded when the saccharine solution is boiled with liquor potassæ and a saturated solution of picric acid, as compared with the tint of a standard of comparison (see under Diabetic Urine).

CHAPTER XIV.

INOSIT.

INOSIT, $C_6H_{12}O_6+2H_2O$.—This saccharine body is met with in the muscle substance of the heart, and in most of the organs of the body, as the brain, liver, spleen, lungs, kidneys, etc.; it has been separated from horse's flesh, the blood of the ox, and the fluid of hydatid tumors; traces of it exist also in most diabetic urines, and it has been noticed in a few cases of diabetes completely or partially to replace the grape sugar, and in about 17 per cent. to accompany the grape sugar; further, it has been found occurring in some 8 per cent. of the cases of Bright's disease, and has been detected even in healthy urine (**Cloëtta**, **Külz**), especially after abundant ingestion of water or the use of diuretics.

Preparation. 1. *From the Juice or the Watery Extract of Muscle.*—First coagulate the albumen by boiling the fluid after the addition of acetic acid; then add baryta water to the filtrate to precipitate the phosphates; filter, and throw down excess of baryta with dilute sulphuric acid; concentrate the filtrate, which causes kreatin to crystallize out. Next treat the hot decanted liquid with four times its volume of boiling alcohol, and if an abundant precipitate is formed, but adhering to the sides of the vessel, decant off the spirit; while if the precipitate does not settle readily filter the hot liquid through a hot funnel, and leave the filtrate to cool. In 24 hours a crystalline deposit has formed; decant and filter the supernatant liquor; then wash the collected crystals with a little cold alcohol, dissolve them in a little boiling water, and reprecipitate with alcohol. If no precipitate appears on the addition of the excess of boiling alcohol, ether is to be added until it appears, and after the mixture has been well stirred the whole laid aside to crystallize.

Or, after separating the albumen, treat the filtrate with neutral lead acetate, and warm the filtrate from this with basic lead acetate; collect the precipitate after twelve hours and having washed it suspend it in water, and decompose with sulphuretted hydrogen. The concentrated filtrate will yield inosit on concentration, particularly after the addition of alcohol.

2. *From Urine containing it.*—Use several litres of weakly acid urine, and proceed as with the juice of muscle, adding neutral and then basic acetate

of lead. After the precipitate with the last has stood twenty-four hours, decompose it as before with hydric sulphide, filter, and after standing some time decant the clear liquid from the precipitated uric acid into a porcelain capsule, where it is to be evaporated to a syrup and then precipitated with absolute alcohol. The precipitate is to be dissolved in hot water, and three to four times the volume of the latter of alcohol (90 per cent.) added; ether is next poured in until a turbidity is produced, and then the mixture is left for the inosit to crystallize out.

3. It is readily prepared from *French beans*. A watery extract is made, which is evaporated down to a syrup and then precipitated with alcohol; the precipitate is dissolved in water, and the inosit allowed to separate by crystallization (VOHL).

Properties.—Forms large, colorless, efflorescent, monoclinic tables, or fine clinorhombic prisms, generally grouped in rosettes. From its solution in boiling spirit it crystallizes in brilliant little lamellæ somewhat like those of cholesterin. It has a sweet taste, and is easily soluble in water, but insoluble in absolute alcohol and ether.

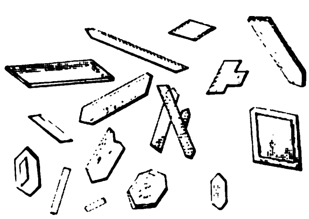


FIG. 14.—CRYSTALS OF INOSIT.

When compared with other sugars many of its properties are negative, thus: it is not decomposed by caustic alkalies or by weak acids; it has no polarizing action on light, neither does it ferment nor reduce metallic oxides; it gives no change of color when boiled with caustic potash, and no reduction of copper with caustic potash and cupric sulphate. Although incapable of alcoholic fermentation it undergoes lactose fermentation when in contact with putrid cheese or decaying animal tissues and chalk, yielding fermentation or sarcolactic (HILGER), butyric, and carbonic acids.

It is precipitated from its solutions by basic lead acetate and ammonia.

Tests.—1. Evaporate a little of its solution containing a few drops of nitric acid nearly to dryness on a platinum dish; treat the residue with a little ammonia and calcium chloride, and evaporate to dryness at a gentle heat: a bright rosy red or violet color is produced (SCHERER). The reaction is delicate, but it only succeeds with pure solutions.

2. Add a drop of silver nitrate to a solution of the inosit in a porcelain dish, and a yellow precipitate is formed. Spread this out carefully on the sides of the dish and heat gently, when it will become dark red or rose-colored; on cooling the color disappears. Albumen, tyrosin, and sugar must be absent (GALLOIS).

CHAPTER XV.

FATS.

Constitution.—Fat is generally a mixture of the neutral fats stearin, palmitin, and olein, the two former of which, being solid at ordinary temperatures, are held in solution by the olein at the temperature of the body. These fats, as we have seen in a previous chapter, are derivatives of the triatomic alcohol glycerin, and may be regarded as organic salts of glyceryl, glycerides, or, as they are termed, compound or glycerin ethers of palmitin, stearin, and olein, in which the hydrogen atoms of the glycerin are replaced by an equivalent of the acid radical. In the fat stored up in or about the internal organs as well as in the fat of marrow there is not so much olein as in the subcutaneous fat.

In the infant body the fatty tissues are firm and hard, and the fat forms a homogeneous, white, solid mass, melting at 45°; it contains more stearic and palmitic acids and less oleic acid than adult fat.

	Infant.	Adult.
Oleic acid	67·75	89·80
Palmitic "	28·97	8·16
Stearic "	3·28	2·84 (LANGER).

Traces of free fatty acids has also been found in human fat by HOFMANN, and as to vegetable fats KÖNIG and BECKE conclude, from their glycerol determinations, that they consist essentially of free fatty acids.

Adipose tissue is made of little rounded or polygonal cells filled with fat. These cells generally lie in groups, and are always in close relationship with the blood vessels. The fat in the cell is not solid during life, and the radiated fine crystalline needles or thin plates occasionally present are most probably *post mortem* in their appearance. These crystals used to be described as *margarin*, but they are really a combination of stearin and palmitin. The fat may also be found in a state of solution, fine subdivision, or admixture with other tissues or fluids throughout the body.

PALMITIN, $C_3H_5(C_{16}H_{31}O_2)_3$ is more abundant than stearin in human fat, and is the chief component of most animal fats, although it also occurs largely in vegetable fats. It is more soluble than stearin in alcohol and ether, but it is only slightly soluble in cold alcohol. It crystallizes in fine needles, and three points of fusion are ascribed to it, 46°, 61°, and 62·8° (DUFFY).

It is readily *prepared* by digesting palm oil repeatedly with alcohol, dissolving up the residue in ether, and repeatedly crystallizing therefrom.

STEARIN, $C_3H_5(C_{18}H_{35}O_2)_3$, is the hardest fat of the body, and also the least soluble or fusible. It is nearly insoluble in cold ether, and, owing to this property, it is possible to obtain pure stearin from suet, in which it is abundant, by filtering the melted suet and extracting it repeatedly with cold ether before dissolving in hot ether, from which it crystallizes out, on cooling, in little mother-of-pearl-like leaflets. Although never found in vegetable fat it occurs in most animal fats to a greater or less extent. It crystallizes from its boiling alcoholic solutions in brilliant quadrangular plates. Stearin melts at 63° to 66°, according to HEINTZ there being two points of fusion, 55° and 71·6°; but the melting point varies considerably, being affected by the application of a high temperature; and it is probable there are three isomeric modifications of it, each with its own melting point, 52°, 63°, and 66°.

OLEIN, $C_3H_5(C_{18}H_{33}O_2)_3$, is a fluid, colorless oil that becomes yellowish when exposed to the air, and is the fluid constituent of most natural fats and fixed oils, dissolving palmitin and stearin in great quantity. It is more abundant in vegetable than in animal fats, and according to some authorities it exists in smaller proportion in human fat than is generally stated. It can easily be *obtained* from olive oil, from which the palmitin has already been in great part separated by cooling the oil down to 0°, then dissolving the fluid residue in alcohol and cooling once again to 0°, when the rest of the palmitin crystallizes out; now dilute the alcoholic filtrate with water, and the triolein will separate.

General Properties.—The fatty bodies are in part liquid and in part crystalline at ordinary temperatures; they are insoluble in water and cold alcohol, but readily soluble in boiling alcohol, also in ether, chloroform, benzol, bisulphide of carbon, and the essential oils; they are slightly soluble in solutions of soaps, albumens, and biliary acids. Dropped on paper they render it transparent, especially when heated. They are readily decomposed by superheated steam under a high pressure, also by the action of boiling caustic alkalies, as soda or potash, being *saponified*, as it is termed, and with ammonia forming ammonia soaps or *liniments*; the oxides of the heavy metals likewise decompose them in a similar way, with the formation of *plasters*. When strongly heated they disengage a characteristic penetrating odor, very irritating to the mucous membrane of the nose and eyes, and due to the formation of *acrolein*, and at a red heat they evolve a mixture of gases, the chief of which are carbonic oxide, hydrogen, marsh gas, and olefiant gas. They decompose slowly in contact with the air and become rancid. In the process of digestion they are subjected to the processes of saponification and emulsion. In the latter the fat is broken up into fine drops, each of which is invested with a thin albuminous coating, and thus maintained apart. The phosphate of soda present in bile is regarded by THUDICHUM as influential in the production of the emulsion in digestion.

Origin and Source of the Fats in the Organism.—Part of the fats is absorbed as such in the intestine, and enters the capillaries in the form of scarcely saponified glycerides, that are subsequently transformed into alkaline soaps. But they also arise in the body at the expense of the albuminoids. It seems doubtful whether any of the fat is derived directly from the sugar absorbed, though this is asserted; but it is probable that the accumulation of fats occurring on a mixed diet rich in sugar is due not to the conversion of the sugar into fat, but rather to the protection thus afforded against the oxidation of the fats. That, however, a large proportion of the fat of fattened animals is not derived from ingested fat, but directly or indirectly from the carbohydrates as well as the nitrogenous elements of the food, particularly when the latter are in excess, seems most probable, and there is no doubt but that a combination of nitrogenous food and saline matter, together with carbohydrates, conduces most to the production of fat in the organism.

From experiments upon geese B. SCHULZE concludes that, as the fat formed was some 20 per cent. in excess of what could be produced by the conversion of the nitrogenous matter of the food, the carbohydrates, under certain conditions, play a distinct part in the formation of fat in the carnivora and herbivora.

When a proteid is broken up we know that one of its derivatives is urea, 100 grams of this body containing as much nitrogen as 300 grams of the proteid; but in addition to this there is a large excess of carbon, etc., to be disposed of, and it is probable that this or part of it, may go to the formation of fat if not immediately required by the organism. Thus VOIT reckoned that 100 parts albumen furnish 33·45 parts urea and 40·08 parts fat, while HENNEBERG gives it as 51·39 per cent. fat, 33·4 per cent. urea, and 27·4 per cent. carbonic anhydride. According to RUBNER, for every 43·3 grams fat 100 grams nitrogenous matter have been destroyed.

The *assigned sources* are therefore: 1. *The fat of the food absorbed as such,* although this accounts for but a small proportion of the stored up fats, some authorities even being of opinion that all the fat taken in the food is directly disposed of. 2. Some is also derived *from the carbohydrates,* a partial convertion of which into fats occurs in the butyric acid fermentation in the intestine. 3. But the *great source seems to be found in the proteids,* although an exclusively proteid diet, from the increased activity of the organic processes, does not tend to cause an accumulation of fat, rather, indeed, the contrary; but it has at least been satisfactorily proved that fat may be derived exclusively from this source.

It should also be remembered that the constitution of the fat of the body does not appear to be modified by the nature of the food; for if an animal is starved, and then largely fed on palmitin, olein, and lean meat, yet stearin will make its appearance in the body fat (SUBBOTIN).

Destination of the Digested Fats.—The fats that are not stored up, or taken up by the tissues requiring them, disappear probably by direct oxidation, being ultimately transformed into water and carbonic acid, and evolving much heat in the process.

Distribution of Fat in the Body.—Fat is one of the most fluctuating constituents of the organism. In the normal condition it is pretty generally distributed throughout the body, and it frequently makes its appearance as a degeneration product of many of the tissues. Besides being enclosed in the cells of adipose tissue, over 83 per cent. of which consists of fat, it is also found free, being met with in this condition in the chyle, blood, lymph, milk, etc. Its proportions in some of the tissues is indicated in the following table:—

	Per cent.
Yellow marrow of bones	96·0
Adipose tissue	82·7
Brain (FRÉMY)	5–8·0
Muscle (BIBRA)	1·5–4·24
Chyle (LIEBIG)	2–2·18
Healthy liver (BOUDET)	1·77
Bone	1·4
Cartilage	1·3
Blood (LECANU)	0·5–0·16
Lymph	0·26–0·05

Tests for the Presence of Fats or Fatty Acids.—1. Wash out a beaker or wineglass very carefully with caustic potash, and then with some boiling alcohol or with ether, and afterwards rinse it thoroughly with water; now place it in a shallow saucer, and fill the beaker or wineglass to overflowing with distilled water. A small bit of camphor, detached from the middle of a freshly broken lump with the point of a knife, which has been washed in ether, is next placed on the surface of the water, when it will be seen to rotate and move rapidly about—a movement, however, that will immediately cease when the slightest trace of oil or fat is brought in contact with it or with the surface of the water.

2. The presence of a free fatty acid is shown by warming the solution containing it with a little rosanilin hydrochloride solution, when a dark red to a reddish black color makes its appearance.

Detection of Fat in a Mixture.—When only a small amount of fat is *present in a mixture* it is best to evaporate it nearly to dryness on a water bath, and to digest the residue with a little warm ether. The ethereal solution is evaporated, when the fat will be deposited, and if this is done on a glass slide very minute traces may be discovered under the microscope, and the particles may be seen to be immiscible with water, and to break up into minute globules when rubbed with a drop of hot water, also to dissolve in warm caustic potash, and to produce acrolein at a high temperature.

In the case of solids dry them thoroughly, reduce them to powder if possible, and then exhaust with ether as above; filter the ethereal extract into a flask, and having added to the filtrate some caustic soda shake well. Any free fatty acids are converted into salts of soda, which dissolve in water, while the neutral fat remains dissolved in the supernatant ether. Decant the latter with a pipette and warm the watery solution on a water bath; then supersaturate with hydrochloric acid, which precipitates the fatty acids. Dissolve up the precipitate in alcohol, and treat the solution with an alcoholic solution of neutral acetate of lead. The precipitate digested with boiling ether gives up oleate of lead, while the palmitate and stearate remain undissolved; but the residue, when decomposed with hydrochloric acid and treated with boiling alcohol, yields free palmitic and stearic acids.

Determination and Separation of Fat.—The tissue, finely divided, is exhausted with boiling ether, and the ethereal solution is evaporated to dryness in a tared capsule, whose increase in weight gives the total fat. DRESCHEL'S apparatus is very convenient for this purpose. The upper flask, which is fitted to the lower one, is in connection with a LIEBIG'S condenser, and contains on a fluted filter the finely divided solid from which the fat is to be extracted. In the lower flask is the ether, whose vapors are condensed in the LIEBIG'S apparatus, and in their way back pass through the upper flask. A constant circulation is thus maintained, and the dissolved fats gradually accumulate in the lower flask.

CHAPTER XVI.

PROTEIDS OR ALBUMINOIDS.

IT has been proposed to define proteids to be nitrogenized colloids, which by hydration split up into amidated acids, carbonic acid, and ammonia (GRIMAUX). These bodies, which chiefly include the albumens, are the most essential to any dietary. When assimilated they are gradually decomposed into simpler compounds, that are burnt up in the economy, passing through a series of transformations, of which the final products are water, carbonic anhydride, and urea.

Where found.—These bodies form the important solid constituents of the blood, nerve, muscle, glands, and organs generally of the body; they also constitute more than half the solids of the gray matter of the nerve centres, and about a fourth of the solids of the white matter of the same: they form, in fact, in combination with much water, and associated with certain acids, bases, and salts, the chief mass of the animal tissues. In all protoplasms there appears to exist a vitellin- as well as a myosin-like body (ROVIDA).

In the normal state such fluids as urine, bile, and tears should be devoid of them.

The albumens seem to exist in a special state of hydration, apt to be modified very rapidly and unceasingly under the influence of variations in the salts dissolved in the different fluids of the economy (GAUTIER).

General Characters.—These albuminous bodies are white, flaky, or granular, and mostly amorphous, and accordingly difficult to obtain pure; they are colloidal—that is, they are not diffusible through parchment paper, and their aqueous solutions polarize to the left, the amount, except in the case of peptones, being altered by heat. Proteid crystals have been met with in white of egg, semen, and in seeds of plants, etc., and it is also possible under certain circumstances to cause proteids to crystallize (DRESCHEL). Some of these albuminoids are soluble and others insoluble in water; they are soluble also in mineral acids and the caustic alkalies, but are almost insoluble in alcohol and ether. They can all become insoluble, either spontaneously, as *fibrin* and *myosin*, or after the action of heat, as *egg-* and *serum-albumen*, or under the influence of weak acids, as *casein*. They also all yield an apparently identical substance, *syntonin*, which is soluble in water containing acid or alkali, but insoluble in neutral liquids; and under the influence of gastric juice they are capable of generating peptones—bodies that are readily assimilable and highly nutritious.

When heated they do not volatilize, but when burnt they give off empyreumatic products having the odor of burnt horn; they likewise putrefy rapidly when exposed to the air. Their solutions polarize to the left, the amount being altered by heat.

Composition, Constitution, and Formulæ of Different Albumens.—Analyses of albumens indicate such a percentage composition as the following (WURTZ):—

C	52·7 to 54·5
H	6·9 " 7·3
N	15·4 " 17·0
O	20·9 " 23·5
S	0·8 " 2·2

Crystalline albumen from hemp seed and ricinus seed gave the accompanying nearly identical numbers (RITTHAUSEN):—

	Hemp. Per cent.	Ricinus. Per cent.
C	50·98	50·88
H	6·92	6·98
N	18·73	18·58
O	22·55	22·79
S	0·82	0·77

Albumens also contain normally a small proportion of lime, that can only be obtained by incineration and is not removable by acids.

According to SCHÜTZENBERGER, albumen is a complex ureide—a derivative of urea and oxamid, and containing ¼ its nitrogen in the form of urea—and possibly it may be regarded as a complex combination containing amidated acids united to an acid x ($C_4H_7NO_4$) minus the elements of water. It decomposes into ammonia, carbonic anhydride, oxalic and acetic acids, and a nitrogenous residue from which the amidated acids, etc., are derived. LIEBIG and GERHARDT considered albuminoid bodies to be isomeric—that is, of the same composition, but differing in their molecular arrangements—while EISCHWALD regarded them as formed of one and the same substance, modified by combining with colloids and crystalloids.

As to *formulæ*, they are untrustworthy and purely empirical. LIEBERKÜHN assigns albumen the formula $C_{72}H_{112}N_{18}O_{22}S$, to its monatomic metallic combinations $C_{72}H_{111}R'N_{18}SO_{22}$, and its diatomic $C_{144}H_{222}R''N_{36}S_2O_{44}$, R indicating the metal. LOEW gives it as $C_{72}H_{108}N_{18}O_{22}S$, while SCHÜTZENBERGER raises the numbers to $C_{240}H_{392}N_{65}O_{75}S_3$.

The percentage composition of some of these proteids is given in the subjoined list:—

	C	H	N	O	S	Authority.
Albumen (of egg) .	52·9	7·2	15·6	23·9	0·4	WURTZ and MULDER.
Gluten . . .	53·5	7·5	14·6	24·4	—	RITTHAUSEN.
Syntonin (of muscle)	54·06	7·28	16·05	21·5	1·11	LIEBIG.
Casein (of milk) .	53·5	7·1	15·8	22·7	0·9	DUMAS, VERDEIL.
Fibrin (of blood) .	52·7	7·0	16·6	22·2	1·5	DUMAS, RÜLLING.
Vitellin (of yolk) .	52·3	7·3	15·1	24·1	1·2	GOBLEY.
Hæmoglobin . .	53·85	7·3	16·17	22·3	0·39	Fe=0·43, HOPPE SEYLER.

Combinations.—Albumen forms a series of definite combinations with acids, as $C_{72}H_{112}N_{18}O_{22}S + 2HCl$ and $C_{72}H_{112}N_{18}O_{22}S + H_2SO_4$. LOEW describes a series of combinations with nitric acid, etc., of which the trinitro-albumen is an example: $C_{72}H_{105}(NO_2)_3N_{18}SO_{22}$.

It also combines with bases, as $C_{72}H_{112}N_{18}SO_{22}+K_2O$; but it must be confessed that the true constitution and molecular weight of such bodies are as yet only imperfectly known.

Derivatives.—Almost all proteids furnish certain derivative amides, named *leucin* and *tyrosin*. When 100 parts of a dry proteid are boiled for several hours with an excess of sulphuric acid diluted with one and a half time its weight of water, leucin and tyrosin will be furnished in the following proportions:—

	Leucin.	Tyrosin.
Albumen of egg	10	1
Syntonin of muscle	18	1
Fibrin of blood	14	0·8
Horn	10	3·6
Elastic tissue	36–45	0·25

Other important derivatives are glycocin ($C_2H_5NO_2$), aspartic acid ($C_4H_7NO_4$), and glutamic acid ($C_5H_9NO_4$). All proteids, when boiled with dilute sulphuric or hydrochloric acid and a little stannous chloride, are exactly resolved into aspartic and glutamic acids, leucin, tyrosin, and ammonia, and may therefore be regarded as formed by the combination of these bodies with elimination of water (HLASIWETZ and HABERMANN).

As the result of their final oxidation in the body albumens yield water, carbonic anhydride (CO_2), and urea $\left(CO\begin{matrix}NH_2\\NH_2\end{matrix}\right)$. What the intermediate products may be we do not yet know, though we are familiar with some of them, such as leucin and tyrosin, as well as such carbohydrates as glycogen ($C_6H_{10}O_5$), and fats. The term metabolism, it may be said, is applied to such a series of chemical transformations as a body like albumen undergoes in its passage through the organism.

When heated with water and bromine under pressure, albumen furnishes bromanilin (1·5 per cent.) and tribromacetic acid (22 per cent.), both secondary tyrosin products; also bromoform (30 per cent.), oxalic acid (12 per cent.), aspartic acid (23·8 per cent.), and leucin (22·6 per cent.), etc., etc.

On exposure to the air these albuminoids putrefy readily, fine granulations developing in their interior, which change into vibrios, oxygen at the same time being absorbed, carbonic anhydride, nitrogen, hydrogen, sulphuretted hydrogen, ammonia, etc., being disengaged, and a series of simple bodies, such as leucin, fatty acids, and tyrosin, being formed. As PASTEUR has shown, these little organisms, which are the excitants of all fermentative and putrefactive processes, are derived from the air, and require a certain supply of oxygen for their development: accordingly, if they are excluded, destroyed, or deprived of the supply of oxygen necessary for the manifestation of their properties, then even such an unstable body as albumen may be long preserved unchanged. The most important fermentation of albuminoid matter is occasioned by *bacterium termo*, and it is this bacterium that induces the decay of all organic matter (MARPMANN).

Stated generally, we may thus sum up some of the albumen derivatives: *albuminates*, by the action of acids and alkalies; *coagulated albumen*, by boiling its solutions or by the prolonged action of alcohol; *peptone*, by the action of pepsin in presence of a dilute acid, which, when trypsin and a dilute alkali are used instead of the acid pepsin, partly splits up into *leucin* and *tyrosin*. When a mixture of albumen and pancreas is allowed to decompose, *indol*, *skatol*, *phenol*, *butyric* and *valerianic acids*, *leucin* and *tyrosin* appear. Early in the decomposition, before indol shows itself, *hypoxanthin* is formed.

Most of the immediate decomposition products of albumen, then, are amides, or bodies that may be regarded as derivatives of one or more molecules of an ammoniacal salt: thus we have glycocin and leucin; amides with aromatic radicals, as tyrosin; and sulphamides, like cystin; as well as acids and aldehydes corresponding to the preceding amides. Sometimes the derivative contains sulphur in place of one of the other elements. In *taurin* or *isethionamide* the sulphur is combined with oxygen, $SO_2\left\{\begin{matrix}C_2H_4.OH\\NH_2\end{matrix}\right.$; while in *cystin* it replaces the oxygen and saturates the carbon, $(C_3H_3S)'''\left\{\begin{matrix}OH\\OH\\NH_2\end{matrix}\right.$.

Certain proteid derivatives, such as protagon and lecithin, contain phosphorus, this element playing the same part as in phosphoric acid $\left(H_3PO_4 = PO\left\{\begin{matrix}OH\\OH\\OH\end{matrix}\right.\right)$. Glycero-phosphoric acid, for example, one of the decomposition products of protagon and lecithin, may be thus expressed: $PO\begin{matrix}OH\\OH\\O[C_3H_5(OH)_2]\end{matrix}$.

a. *Among these decomposition products at least three aromatic groups are present:—*

1. The *phenol group*—tyrosin, the aromatic oxyacids, phenol, and kresol. The tyrosin does not appear as such in normal urine, but its decomposition products present themselves.

2. The *phenyl group*, as phenylacetic and phenylpropionic acids. The latter is oxidized to the state of benzoic acid, and appears in the urine as hippuric acid (SALKOWSKI).

3. The *indol group*, as indol and skatol. In an oxidized form, and combined with sulphuric acid, these two bodies appear as indican and skatoxyl-sulphate.

β. *As well as a group belonging to the fatty series*, and including such bodies as leucin, aspartic acid, and hypoxanthin.

Origin, Destination, and Theories as to the Terminal Products of the Decomposition of Albumen.—Under the influence of the solar rays plants decompose the carbonic anhydride in the atmosphere, evolving the resulting oxygen and fixing the carbon. A series of other reactions also occur in the plant in which higher and more complicated bodies are formed at the expense of simpler bodies, such as water, ammonia, and the like. While we may theorize as to the general nature and direction of these reactions we are as yet ignorant as to their exact character or their order of succession. But, as their result, in the laboratory of the plant from simple bodies spring bodies of more complex constitution, until we arrive at the albumens, in which is stored up the great amount of energy expended in their elaboration.

These vegetable albumens are subjected to certain changes in the stomachs of the animals feeding upon them, by which somewhat simpler bodies, capable of dialysis, are formed. To these so-called *peptones* THIRY gives the composition C=15·34, H=7·25, N=16·18, S=2·12, O and P=23·11, which would seem to indicate that a substance of the nature of leucin had been separated.

When absorbed as peptones or albuminates, and thus introduced into the blood, probably some combination occurs between these bodies and the alkalies and salts of the plasma, and in this condition possibly the tissues requiring albumen are nourished. Some of the absorbed substance unites with new elements to form hæmoglobin, but the greater part undergoes retrograde metamorphosis, passing from a complex condition to a series of simple combinations, and evolving its energy in doing so. Fats, glycogen, mucin, and the collagens generally probably result from some of these alterations. Early derivatives are possibly asparagin and kreatin, bodies that are closely allied:

Asparagin	$C_4H_8N_2O_3$
Kreatin	$C_4H_9N_3O_2$.

Guanidin also has been obtained as an oxidation product (LOSSEN). The different changes are gradual and progressive. This is well seen in the bodies sarkin, xanthin, and uric acid, which afford a marked example of this successive oxidation:

Sarkin	$C_5H_4N_4O$
Xanthin	$C_5H_4N_4O_2$
Uric acid	$C_5H_4N_4O_3$.

The sarkin, which is one of the higher albuminoid derivatives, in being oxidized gives rise in succession to xanthin and uric acid; and we may trace the decomposition still further, as shown in these reactions:—

$$\underset{\text{(Uric acid.)}}{C_5H_4N_4O_3} + H_2O + O = \underset{\text{(Allantoin.)}}{C_4H_6N_4O_3} + CO_2$$

$$\underset{\text{(Allantoin.)}}{C_4H_6N_4O_3} + 2H_2O + O = \underset{\text{(Oxalic acid.)}}{C_2H_2O_4} + \underset{\text{(Urea.)}}{2CON_2H_4}$$

$$\underset{\text{(Oxalic acid.)}}{C_2H_2O_4} + O = 2CO_2 + H_2O$$

From sarkin we thus come by gradual stages to its final decomposition products, urea, carbonic acid, and water.

Kreatin, xanthin, hypoxanthin, and the biliary acids are all generally regarded as decomposition products of the albumens; but as to the kreatin, which is so generally distributed through the organism, being a direct predecessor of urea, there is still some doubt.

According to **Schultzen** and **Nencki**, albumen is decomposed into certain bodies belonging to the amido-acid series which pass into urea, while the non-nitrogenous part of the albumen may pass into the fatty series. They were further of opinion, in which they are supported by **Hoppe Seyler** and **Salkowski**, that in the passage from albumen to urea cyanamid is probably formed. Under the influence of strong acids and alkalies albumen gives rise to leucin (amido-caproic acid, $C_6H_{13}NO_2$), aspartic acid [amido-succinic acid, $C_4H_7NO_4$ or $C_2H_3(NH_2)(CO.OH)_2$], tyrosin, $C_9H_{11}NO_3$, and glycocin (amido-acetic acid, $C_2H_5NO_2$). Somewhat similar substances are obtained by the prolonged action of trypsin on albumen or gelatin.

Schmiedeberg is of opinion that the nitrogen of the albumen passes out as ammonic carbonate, and that this, by the removal of water, forms urea. **Danilewsky** has obtained a crystalline compound having the composition $C_{21}H_{26}N_2O_8$ on subjecting peptone, egg albumen, etc., to the continued action of pancreas ferment. In its chemical reactions it partakes of the properties of both tyrosin and inosit, but it has a less stability than either of these bodies.

Dreschel supports the view that the amido-acids pass over into carbamic acid, two molecules of which form urea:

$$2CO\begin{cases}NH_2\\OH\end{cases} = CO\begin{cases}NH_2\\NH_2\end{cases} + CO_2 + H_2O.$$

Traces of this carbamic acid he discovered in the blood. Salts of carbamic acid, he also finds, are formed by the oxidation of glycocin; and he considers it probable that ammonic carbonate is the immediate source of urea by the removal of the elements of water. In dogs, for example, it has been shown that ammonic carbonate and acetate are converted into urea (**Hallervorden** and **Voit**). In the formation of urea from albuminoids **Dreschel** concludes that these bodies are first resolved into glycocin, tyrosin, leucin, etc., and that these in turn are oxidized into carbamates, that are finally converted into urea under the influence, possibly, of some ferment.

According to **Cazeneuve**, the proportions existing among the amounts of uric acid, urea, and ammonia, excreted by birds are not influenced by an increase or decrease of oxidation, but he finds that the total amount excreted varies with the quantity of nourishment taken; from which it might be concluded that the albuminoid matters in the system undergo a decomposition depending on hydration rather than on oxidation.

CHAPTER XVII.

THE PROTEIN REACTIONS AND ALBUMEN TESTS.

THE PROTEIN REACTIONS.—Protein was a hypothetical radical supposed by MULDER to exist in all albuminoid principles; and as the three following tests apply to all such bodies, they received their designation accordingly.

1. *A blue or violet coloration* is obtained by adding to the albuminoid in solution a few drops of sulphate of copper solution, and then an excess of caustic soda. The violet color deepens on boiling, but no other change is produced. The same result is had by the addition of a few drops of Fehling's solution. In the case of a solid albuminoid, touch it successively with the sulphate of copper and the caustic soda, and then wash the touched surface, when it will be found to be stained of a violet color. The coloration can also be well shown by shaking, say, a piece of fibrin, in some very dilute solution of cupric sulphate, when the latter will become colorless, the fibrin taking a greenish tint, which, however, becomes violet when the fibrin is shaken up with some caustic alkali like lime, or baryta water, or caustic potash.

2. *The xanthoproteic reaction, or yellow coloration*, got by the action of strong boiling nitric acid, which is changed to an orange or amber-red color, by the addition of ammonia to the liquid when cold.

3. *A rose or red coloration* by heating with Millon's reagent, which is changed to an orange by caustic potash. Unless the solution is very dilute a red precipitate appears.

Preparation of an Albumen Solution for Testing.—Take several eggs, and having made a small hole in each end, allow the white to escape into a dish, taking care to let none of the yolk escape. With a pair of scissors cut up the albuminous fluid thus collected, so as to divide freely the network of fine membranes in which the albumen is enclosed; next stir up the mass rapidly with twice its volume of water, and strain through a linen cloth.

The albumen thus obtained will serve for testing; but if it is required *pure*, then the following method may be adopted: Shake it well in a flask, skim off the white froth, and express through a linen cloth; add dilute acetic acid to the filtrate so long as any precipitate is formed, and filter first through a piece of fine muslin and then through filter paper, making use of a series of small filters under a bell jar that is kept charged with carbonic acid gas. Then dialyse the filtrate for a couple of days, renewing the outside water frequently; dilute the contents of the dialyser with three times their volume of water, pass a current of carbonic acid through the mixture, and filter if necessary. But for ordinary analytical purposes the dialysis may be left undone, and the filtrate merely neutralized carefully and concentrated somewhat at a temperature not higher than 40°.

To prepare a solution of serum albumen, which is the most frequent form present in albuminous urine, if the latter fluid cannot be obtained, then to serum of blood or hydrocele fluid add very dilute acetic acid with constant stirring till a flocculent precipitate is obtained; filter and nearly neutralize the filtrate with a dilute solution of sodic carbonate; evaporate to a small bulk about 40°, then dialyse for several hours to separate the salts, and evaporate to dryness at 40°. A solution of this will serve the purpose.

Although some observers are disposed to regard serum and egg albumen as almost identical, yet there are really some differences, which will be referred to before the general tests for albumen are given in detail.

With dilute solutions it will be found that—

1. *Egg albumen* is coagulated by ether.	*Serum albumen* not coagulated.
2. Egg albumen is readily precipitated by hydrochloric acid, the precipitate not dissolving in excess.	Serum albumen not precipitated so readily, but the precipitate, when formed, redissolves in slight excess of the acid.
3. Egg albumen gives a precipitate with nitric acid, which is with difficulty soluble in excess.	Serum albumen gives a similar precipitate, which is readily soluble in excess.

General Tests and Reactions.—1. *Boiling precipitates albumen solutions.* The coagulation thus effected requires the presence of water, as dry soluble albumen is not coagulated or rendered insoluble by being exposed to a temperature of 100°.

The *temperature at which the coagulation occurs varies* with the different albumens, but it averages from 60° to 75°; the presence of a little free acid, or of a neutral alkaline salt like sodium chloride, causes the coagulation to occur at a lower temperature; the presence of an alkali, at a higher temperature, while if much alkali is present no coagulation will take place at all.

Take six test tubes with some simple albumen solution in each; add a few drops dilute acetic acid to the first, a little of the same acid and some sodic chloride or sulphate to the second, a little sodic carbonate to the third, a considerable excess of caustic potash or ammonia to the fourth, a few drops of neutral solution of litmus to the fifth, and nothing to the sixth. Each tube should have a label attached to it. Next place the six test tubes in a beaker containing water, and immerse the beaker in a water bath. Watch the tubes while they are being heated; coagulation first shows itself in the tube containing acetic acid and the salt, next in the acidified albumen, then in the simple albumen solution, and lastly in the sodic carbonate tube, while no coagulation will occur in the tube containing excess of caustic potash, unless first neutralized with an acid; and in the tube to which litmus was added a blue color will make its appearance on the coagulation of the albumen, owing to the alkali set free in the process.

2. *Of the mineral acids nitric, metaphosphoric, and phosphotungstic precipitate albumen most completely.* 1 part of albumen in 100,000 parts of water can be identified by the last acid (HOFMEISTER). Ordinary phosphoric acid does not precipitate it.

If only a trace of albumen is present, as is often the case with albuminous urine, it is best to place the liquid in a test glass, and then slowly and carefully pour some strong nitric acid down the side of the tube, so as to form a layer at the bottom. A *white cloud* will show itself at the line of junction of the two fluids. This will be readily seen by holding the vessel in a clear light and moving it up and down about the level of the eye. Or, if only a little of the urine is procurable, I have been accustomed to apply this modification of the nitric acid test with a small glass syringe, first drawing up the urine and then the acid.

3. (*a*) *Of the organic acids carbolic, picric, and tannic act as precipitants.* By using the picric acid in the same way as the nitric acid in the preceding paragraph, very delicate results can be obtained. But with none of these acids is the precipitation complete in the presence of alkalies or their carbonates.

(*b*) *Acetic acid and ferrocyanide of potassium* give a white flaky precipitate, which is somewhat soluble in excess.

(*c*) *Acetic, tartaric, and citric acids*, in presence of *excess of a cold saturated solution of a neutral salt* like sodium chloride or sulphate, or of a body like *gum* or *dextrin*, precipitate albumen.

The albumens with the exception of casein and syntonin, are not precipitated by acetic acid alone.

4. *Salts of heavy metals, such as silver, mercury, lead, and copper,* throw down albumen from its solutions. Basic lead acetate precipitates it abundantly, the normal acetate only slightly. Tungstate of soda and potassio-mercuric iodide are also very delicate precipitants.

5. Other precipitants are *freshly prepared ferric acetate*, *carbonate of potash* to saturation, *alcohol*, and *aceton*. A solution of *taurocholic acid* also precipitates albumen and syntonin, but *not peptone* or *propeptone;* all the other delicate reagents for albumen also precipitate the peptones.

6. *Color Reactions.*—

(*a*) All the albuminoids, when *dissolved in glacial acetic acid*, give on the addition of *strong sulphuric acid*, *violet blue*, *slightly fluorescent solutions*, and when sufficiently concentrated produce an absorption spectrum between b and F like urobilin and choletelin (ADAMKIEWICZ). The presence of sodic chloride strengthens the reaction, but that of iodine spoils it. With peptones the coloration is well marked.

(*b*) Albuminous solutions show a green fluorescence with reflected light, which disappears on the addition of acetic acid in excess. If the albumen is precipitated with silver nitrate, and the precipitate dissolved in a mixture of equal parts of *acetic and sulphuric acids*, the color of the solution rapidly passes from violet through red and orange to yellow; but the addition of fresh sulphuric acid causes the violet color to be restored in the inverse order.

(*c*) When albumen is dissolved in *strong sulphuric acid* alone a solution, differing in color according to the quantity of reagent employed and to the amount of albumen present, will be obtained: thus 1 c.c. pure sulphuric acid (sp. gr. 1·809) gives with 1·5 per cent. albumen a greenish yellow, with 7 per cent. an orange, with 15 per cent. a red, and with 22 per cent. a violet solution.

(*d*) When a little albumen is floated on or dissolved in water, a little sugar solution poured in, and then some concentrated sulphuric acid added carefully and with constant shaking, a purple violet or beautiful red coloration is produced (SCHULTZE).

(*e*) When acted on with a *mixture of sulphuric and molybdic acids* an *intense blue* is developed (FRÖHDE).

(*f*) Concentrated *hydrochloric acid* dissolves it at a gentle heat, a blue, violet, and lastly a brown coloration being produced, and a precipitate falling on neutralization. By warming the albumen with hydrochloric acid to which a few drops of strong sulphuric acid have been added a violet liquid results.

(*g*) *Iodine* strikes a brownish yellow, and *nitric acid* a yellow coloration; the latter is changed to a reddish orange by the addition of caustic soda.

(*h*) Mix the albuminous body with a little dilute solution of cupric sulphate, add some caustic potash or soda, and warm; a beautiful violet color is produced.

These color reactions can be characteristically obtained with mere traces of albumen on slides when examined microscopically.

(*j*) Precipitate albumen with chloride of gold, and dissolve the precipitate in a mixture of equal parts of acetic and sulphuric acids; the red solution, like the solutions of metallic precipitates of albumen, shows a broad band between E and F; and a similar band is given, as we have seen, with the solution of albumen in acetic and sulphuric acids.

Alteration of Albumen by the Action of Acids and Alkalies.—The albumens are converted into *albuminates* by these reagents: *alkali albumen* by allowing the albumen to stand some time with a caustic alkali, the conversion being accelerated by a gentle heat; and *acid albumen* by treating a solution of albumen with very dilute acids, or dissolving solid albumen in strong acids.

(*a*) *Alkali Albuminate.*—1. Add to the solution of albumen a few drops of caustic potash, and warm *gently* for a few minutes; then boil, and it will be found that no coagulum occurs.

2. To a little of the above solution, when cooled, add a drop of litmus solution, and neutralize carefully by the addition of dilute hydrochloric or acetic acids; a precipitate falls, that dissolves in excess of hydrochloric acid.

3. Boil a little solid alkali albumen (see preparation, p. 115) with water, and test some of the solution with a current of carbonic anhydride, when a precipitate will fall; to another portion add powdered magnesic sulphate to saturation, and a precipitate is formed; and add alcohol to a third, when no precipitate will appear.

4. To some of the alkali albuminate solution add a little sodic or potassic phosphate, next a few drops of litmus solution, and then neutralize with dilute acetic acid: *no precipitate will occur until an excess of acid is present*, as indicated by the red coloration of the litmus. But a precipitate may also be obtained by boiling the neutralized solution, owing to the conversion of the acid phosphate produced in the reaction into neutral phosphate, free acid being thus liberated.

(*b*) *Acid Albuminate.*—1. Place a little solution of albumen in a beaker, add to it an equal volume of dilute hydrochloric acid (0·5 per cent.), and lay aside for some hours, when the albumen will be converted into acid albuminate; but the conversion is much accelerated by the application of a very gentle heat.

2. Boil a little of the solution thus obtained; no precipitate occurs. A dilute solution of albumen, slightly acidified, if very gradually brought up to boiling point, may in like manner give no precipitate.

3. Neutralize a little of the albuminate solution of 1 with dilute caustic potash solution: a precipitate is thrown down. *The presence of an alkaline phosphate does not interfere with the precipitation.*

4. Dissolve a little syntonin in lime water; boil half the solution, and a coagulum will be obtained; but the addition of powdered sulphate of magnesia to saturation to the other half causes no precipitate to appear, although it shows itself on boiling.

The presence of nitrogen and sulphur in albumen may readily be shown by placing a bit of dried albumen or fibrin in a reduction tube, and inserting in its mouth a piece of red litmus and a bit of paper prepared with plumbic acetate; then heat the tube, and after a little it will be seen that the litmus becomes blue and the lead paper black.

Detection of Albumen in an Animal Fluid.—1. Test the reaction. If *too acid* add a little dilute caustic soda without rendering it alkaline, then add sodic sulphate and ammonic chloride or a neutral salt of the alkalies, and boil. If *alkaline* neutralize with a few drops of acetic acid, carefully avoiding an excess, and boil as before. Precipitates will thus be obtained.

2. Test some of the solution with a little dilute nitric acid.

3. Confirm by testing with tannic acid and mercuric chloride; or with picric acid, tungstate of soda, or potassio-mercuric iodide.

Separation of Albumen from its Solutions.—1. Acidify with acetic acid the fluid containing the albumen, and add an equal volume of a concentrated solution of sodic sulphate; then boil. In this way albumen can be separated from sugar and the like without interfering with the after-detection of these bodies.

2. The separation may be effected by boiling with acetic acid alone, avoiding excess, and any albumen still remaining in the filtrate may be completely removed by again boiling it after the addition of a little freshly prepared acetate of iron, obtained by saturating acetic acid with ferric hydrate. Hydrated oxide of lead at boiling point also separates it completely.

3. Acidify strongly with acetic acid, and add twice the volume of alcohol; filter in 24 hours. This is a good plan when other substances are present which might be decomposed by boiling.

4. Acidify with acetic acid, evaporate to dryness, and treat the dry, pulverized mass with boiling alcohol, ether, and water. The albumens present are thus rendered insoluble.

5. Place the solution in a dialyser immersed in water: crystalloid constituents, such as the soluble salts, sugar, and urea, will pass through the parchment paper, and leave the albumen behind. It is possible in this way to separate serum or egg albumen from paraglobulin, as the latter is precipitated when the salts keeping it in solution dialyse out.

CHAPTER XVIII.

CLASSIFICATION OF ALBUMENS.

I SHALL adopt more or less closely HOPPE SEYLER'S old arrangement, and give at the same time some details as to each variety.

I. **NATIVE ALBUMENS.**—These are soluble in water, and precipitated therefrom by boiling, or by alcohol in presence of alkaline salts, though not in their absence; but not precipitated by very dilute acids, alkaline carbonates, or sodic chloride.

(*a*) **Albumen of Serum** (**Serine**).—This is very widely spread in the animal body, constituting a constant and essential element in all the nutritive fluids of the economy, such as the blood (2·7 to 4·22 per cent.

of the serum, FRÉDÉRICQ), lymph, chyle, milk, serous fluids, muscle juice, etc.; it is also the most frequent form found in the urine in renal affections.

Properties.—Dry serum albumen is yellowish and translucent; its solution, when containing only a small proportion of salts, has a specific rotation of —56° for yellow light (given also as —57·27°). It is not coagulated by ether; nitric and hydrochloric acids precipitate it, the precipitate with the latter being soluble in excess, but reprecipitated on the addition of water. The temperature of coagulation, as we have already seen, is affected by the presence of certain acids and salts; thus in the case of albuminous urine the coagulum may appear below 70°, and even as low as 50° when the urine has an acid reaction, but with an alkaline urine coagulation does not commence till a temperature of 73° is reached.

Dilute acids at ordinary temperatures give no precipitate, but at higher temperatures and with more concentrated solutions the precipitation is evident.

Preparation.—To blood serum or hydrocele fluid add acetic acid drop by drop till a flocculent precipitate is formed; then filter, and having neutralized the filtrate with a little sodic carbonate evaporate to a small volume in a shallow dish at about 40°. Dialyse the concentrated fluid, changing the outside water frequently, and after three or four days evaporate the contents of the dialyser to dryness. Some ash is still present. Or saturate the serum with crystallized magnesic sulphate, filter from the precipitated serum globulin, and dialyse the filtrate till no more chlorides or sulphates can be detected in the dialysate. Then evaporate the contents of the dialyser *in vacuo* over sulphuric acid.

(β) **Albumen of White of Egg.**—It is coagulated when shaken with ether in presence of alkaline salts. Hydrochloric acid precipitates it readily, and when added in excess it gives a coagulum that is with difficulty soluble in the concentrated acid; serum albumen is not only more readily precipitated by but also more easily soluble in hydrochloric acid. If egg albumen is injected hypodermically or into the veins, or introduced in large quantity into the stomach or intestine of an animal in a fasting condition, it is excreted unchanged by the kidneys, which is not the case with serum albumen (STOKVIS). Pure albumen of egg, in which it is probable several albumens may be present, begins to coagulate at 54° to 59°, the coagulation increasing at 63° and 74°, but when mixed with salts the temperature at which this occurs varies considerably. According to MATHIEU and URBAIN, when all the free gas contained in albumen of egg is removed by exhaustion, a liquid albumen is obtained not coagulable by heat.

After its precipitation by the mineral acids or the prolonged action of alcohol, the albumen is coagulated and rendered no longer soluble in water; but the precipitate obtained by mercuric chloride, silver nitrate, or lead acetate is not coagulated, and is soluble on the removal of the precipitant.

Egg albumen is most energetically precipitated by heat, serum albumen by alcohol.

The opportunity may be here taken of giving the chemical composition of a hen's egg (after POLECK, PARKES, PROUT, etc.)

A *hen's egg* varies in weight between 45 and 60 grams. Three parts of it are to be distinguished—the shell, the white and the yolk. The relations among these in weight may be expressed as 1 : 5 : 2·5, but when dried at 100° as 1 : 0·8 : 1·2. The proportion of the yolk to the white varies as 1 to 1·4, 1·6, or 2·09, the white attaining its greatest weight in spring and the yolk in summer.

(j) The *shell*:—

Organic substances	4·15
Carbonate of lime	93·70
" of magnesia	1·39
Phosphate of lime and magnesia	0·76

(ij) The *white*:—

Solids	12–18 per cent.
Water	88–82 "

The solids generally vary about 13·3 per cent., of which some 12·27 per cent consists of albumens, with 0·5 per cent. of grape sugar, and traces of olein, palmitin, sodic oleate and palmitate, and inorganic salts. These salts in 100 parts of ash have this composition:—

K_2O	28·45	SO_3	2·63
Na_2O	27·90	CaO	1·74
Cl	25·20	MgO	1·00
CO_2	11·60	Fe_2O_3	0·44
P_2O_5	4·83	SiO_2	0·49

(iij) The *yolk* contains 44 to 55 per cent. of solids; these are vitellin, nuclein (0·2 to 0·3 gram in an egg), alkali albuminate, lecithin, palmitin, olein, grape sugar, two pigments (lutein), and inorganic salts, especially potassic phosphate.

Water	47·19
Solids	52·81
Albumens	14–15·62
Ether extractives:	
Lecithin	6·80
Fats	22·83
Cholesterin	1·75
Alcoholic extractives	4·83
(Lecithin	3·92)
Nuclein	1·50
Salts:	
Soluble	0·35
Insoluble	0·61

The salts have the following percentage composition:—

Phosphoric acid	63·8–66·7
Lime	12·2–13·2
Potash	8·0– 8·9
Soda	5·1– 6·5
Magnesia	2·0– 2·1
Oxide of iron	1·1– 1·4
Silica	0·5– 1·4

II. **THE GLOBULINS.**—Insoluble in water, all dissolved by dilute sodium chloride solution (1 per cent.), but with the exception of vitellin are precipitated therefrom by saturated solutions of the same, or by the addition of a large quantity of water; soluble also in very dilute hydrochloric acid with the production of syntonin. Its solutions are coagulated by heat (not completely till 93° is reached), and are precipitated by alcohol and even by the weakest acids, such as carbonic, the precipitate, however, disappearing when a stream of air or oxygen is passed through it.

Globulin itself, so called, as found in the blood corpuscles, crystalline lens, etc., is probably an alkali albuminate.

(α) **Vitellin.**—Its solution is not precipitated by the addition of solid sodic chloride in excess. In the yolk of egg it is chemically associated in some way with lecithin.

It is **prepared** by digesting yolk of egg with water and ether so long as any yellow coloration is given; the residue is then shaken up with sodic chloride solution (10 per cent.), which dissolves it, and it is precipitated therefrom by the addition of an excess of water acidulated with a few drops of acetic acid. It may be rapidly dissolved up again and reprecipitated, and afterwards digested with alcohol, so as to purify it.

Vitellin is a white granular body which is very soluble in dilute sodic chloride solutions, but not precipitable therefrom by saturation with solid sodic chloride, coagulating about 70° to 80°; it is also very soluble in dilute hydrochloric acid ($\frac{1}{10}$ per cent.) and in weak alkaline solutions. It is precipitated from its solutions by alcohol, and its neutral solutions heated to 75° are coagulated.

(β) **Crystallin or Globulin.**—This body is not precipitated from its solutions by saturation with sodic chloride, thus resembling vitellin, but it is readily precipitated by alcohol. The crystallin- or globulin-like body precipitated from diluted serum by the cautious addition of acetic acid is said to differ from fibrinoplastin merely by the admixture of fibrin ferment with the latter (WEYL); but although crystallin corresponds very closely with fibrinogen and fibrinoplastin, it has no power, like them, in causing or assisting coagulation.

Preparation.—The lens contains several albuminoid bodies. If it is rubbed up with washed sand and then digested with water a solution is obtained of these; after stirring well, filter, and the paraglobulin can be separated by passing a current of carbonic anhydride through the filtered liquid.

This paraglobulin is also precipitated by dilute acetic acid, and when thus precipitated it is insoluble in water containing no air dissolved in it, but if some oxygen is passed through the water it soon forms an opalescent solution. On heating this solution to 93° a coagulum separates, but the filtrate will not pass through clear unless some neutral salt of the alkalies has been added previous to heating.

(γ) **Myosin,** or *Muscle Fibrin.*—Its sodium chloride (10 per cent.) solution is precipitated by solid sodic chloride added in excess, or by extreme dilution with water. It is soluble in dilute hydrochloric acid, dilute alkalies, and neutral saline solutions. It is coagulated by heat (55° to 60°), and precipitated and afterwards coagulated by alcohol. After being dried its solubility is lessened. Between globulin and fibrin it is intermediate in its characters, like fibrin under certain conditions decomposing hydrogen dioxide, and giving a blue color with the guaiacum test.

Myosin is the name given to the solid body that separates in the coagulation of muscle plasma, and forms an elastic gelatinous clotted mass.

To obtain muscle plasma several large frogs are bled, and their blood vessels are washed out with a sodic chloride solution (0·5 per cent.); the muscles are then removed, cut into pieces, and again washed in the salt solution, the temperature being kept down to 0°. The fragments are next tied up in a linen cloth, placed in a tin or platinum crucible inserted in a freezing mixture of equal parts of snow or pounded ice and salt; when frozen hard the mass is cut into thin slices with a sharp knife that has been lying in the freezing mixture, and then pounded in a cooled mortar. Now tie up the broken muscle in a linen cloth, and express powerfully into a vessel surrounded by ice, the expressed fluid being filtered through a series of filters moistened with the saline solution (½ per cent.) into a cold beaker; and it is advisable to place the glass funnel in a larger metal funnel, filling the space between with snow and salt.

The preparation of the plasma by the above process requires much dexterity, and must be done rapidly, and the temperature kept low all the time. The muscles of frogs are used in preference to those of mammals, on account of their coagulation setting in more slowly.

The *muscle juice* is slightly yellow, opalescent, and syrupy, has a faint alkaline reaction, and coagulates at ordinary temperatures, becoming first a solid jelly and then separating into a loose and granular clot and an acid serum. The clot is myosin. The separation of myosin from muscle plasma is also readily effected by the addition of very dilute acids or sodic chloride solutions above 10 per cent.

The *muscle serum*, obtained by the separation of myosin from the muscle plasma, contains three albumens—a potash albuminate like casein, precipitated by the addition of an acid at 20° to 30°; a serum albumen in large amount, coagulating at 75°; and an albumen or albuminate coagulable at 45° and insoluble in salt solutions.

Myosin is much more easily prepared in this way. Some finely divided muscle is thoroughly washed in water, and then triturated well in a mortar with a solution of ammonium chloride (12 to 15 per cent.); after several hours it is strained and subsequently filtered through paper, and the solution allowed to fall drop by drop into a tall vessel filled with distilled water. The myosin separates in small flocks (DANILEWSKY).

Syntonin is readily formed from myosin, a solution of the latter in a very small quantity of hydrochloric acid being converted into syntonin on heating it to 50°–55°. A reconversion can also be effected by dissolving the syntonin in lime water, adding dry powdered ammonium chloride in excess, filtering, and cautiously neutralizing the thick alkaline opalescent solution with acetic acid. This solution behaves like a freshly prepared solution of myosin in ammonium chloride solution.

(δ) **Fibrinogen** (Metaglobulin).—*Denis' Plasmin* is probably a mixture of paraglobulin and fibrinogen.

(ε) **Fibrinoplastin** (*Kühne's Paraglobulin*, *Panum's Serum Casein*).—Both these bodies comport themselves like myosin, but form fibrin when their neutral solutions are mixed in presence of a special ferment.

Like myosin they also decompose hydrogen peroxide. They are soluble in acetic acid, dilute alkalies, alkaline carbonates, and neutral saline solutions, and are reprecipitated therefrom by carbonic acid or very dilute acetic acid ($\frac{1}{10}$ per cent.). The solutions in dilute alkalies are not coagulated by heat, and the respective solutions of these two bodies in 1 to 5 per cent. sodic chloride solutions behave differently when heated—the fibrinoplastin coagulating at 68° to 70° or 75°, the fibrinogen at 52° to 55° (HAMMARSTEN). According to the same observer a further great distinction between these two bodies is, that paraglobulin is not altered by the action of fibrin ferment, while the fibrinogen is converted by its agency into fibrin.

Where found.—*Fibrinoplastin* is met with in the serum of blood after coagulation has occurred, and is present in the corpuscles, chiefly the pale (in bullock's blood forming 3·58 per cent. and in rabbit's blood 1·26 per cent., FRÉDÉRICQ), also in lymph, chyle, pus, and some serous fluids, in connective tissue, and in the cornea. *Fibrinogen* exists in blood, chyle, and lymph, and in serous fluids generally, but particularly in hydrocele and pericardial fluids, the latter being specially rich in it. Some fibrinogen as well as serum globulin and albumen are present in dropsical effusions. These do not, however, coagulate spontaneously, but yield fibrin on the addition of fibrin ferment or on heating to 60°.

Preparation.—I. *Both bodies* can be thus separated in succession from the blood of the horse: Collect the blood, lay it aside in the cold (below 0°) for an hour to allow the corpuscles to sink, and decant the plasma. Dilute this with ten times its volume of iced water, and then pass a current of carbonic acid through it. The flocculent or somewhat granular precipitate is *fibrinoplastin*. After decantation and filtration dilute the filtrate with twice its volume of water at 0°, pass more carbonic acid, and neutralize with dilute acetic acid. A viscous precipitate will be obtained of *fibrinogen*, which can be purified by washing it with carbonated water. The temperature must be kept down to freezing point all the time. It will thus be seen that in preparing fibrinogen the fluid is more strongly diluted than in the preparation of fibrinoplastin, and the current of carbonic acid must be passed for a longer time.

By saturating the plasma with sodium chloride added in powder a precipitate is obtained containing *both fibrinoplastin and fibrinogen*. Wash the precipitate by decantation with saturated solution of sodium chloride, and filter rapidly at a low temperature. The filtrate will soon coagulate.

II. *Fibrinoplastin* alone can be prepared readily by diluting serum with 15 times its volume of distilled water and adding a little dilute acetic acid (25 per cent.)—about 3 or 4 drops of this to every 10 c.c. of serum employed. The diluted serum may likewise be precipitated with excess of sodium chloride in powder. The fibrinoplastin thus obtained possesses the greatest fibrinoplastic properties.

Or dilute serum with ten volumes of water, and pass a stream of carbonic acid through it for half an hour, keeping the temperature as low as possible. Lay aside for 10 or 12 hours, decant carefully the supernatant liquid, filter, and wash the white, finely granular precipitate thoroughly with carbonated water. This operation is to be recommended.

HAMMARSTEN states that the whole of the fibrinoplastin is not obtained by any of these methods, but he considers that this can be effected by the addition of magnesium sulphate to saturation.

But it is even doubtful whether the whole of the precipitate thus obtained should be termed fibrinoplastin. That they are of the nature of globulin there seems to be no doubt, so that it is capable of reacting with fibrinogen we may safely speak of it as fibrinoplastic globulin. It is insoluble in water and in concentrated saline solutions, but soluble in dilute saline and alkaline solutions, being precipitable therefrom by a current of carbonic anhydride or the addition of very dilute acetic acid. While the solutions in the dilute alkalies do not coagulate when heated, this occurs with the sodic chloride solution.

III. *Fibrinogen* is more difficult to prepare than fibrinoplastin. HAMMARSTEN obtains it thus from blood: Collect the blood of a horse in a vessel containing a saturated solution of sulphate of magnesia—in the proportion of four volumes of blood to one of the saturated solution. Leave aside for several days and filter; add to the filtrate an equal volume of saturated solution of sodium chloride, and the fibrinogen is precipitated. To purify it the precipitate is well pressed between folds of filter paper, redissolved in 6 to 8 per cent. sodium chloride solution, and reprecipitated by a saturated solution of the same salt: this process is repeated two or three times, when the precipitate will be free from paraglobulin and serum albumen.

Fibrinogen, however, is more easily prepared from a serous exudation like hydrocele fluid, by diluting this with ten volumes of water, and passing a stream of carbonic acid through the diluted fluid for about half an hour. The same method of preparation, therefore, applies to fibrinogen and fibrinoplastin, but with the former a greater degree of dilution is necessary, as well as a longer passage of the gas through the liquid.

The same precipitate is also obtained by diluting the hydrocele fluid with 10 to 20 volumes of water, and exactly neutralizing with very dilute acetic acid. The precipitate is flaky and viscid, and adheres to the walls of the containing vessel.

It can likewise be separated by the addition of a mixture of alcohol (3) and ether (1).

This fibrinogen is insoluble in water or saturated solutions of sodium chloride or magnesium sulphate, but is soluble in dilute solutions of the neutral salts of the alkalies and in very dilute solutions of the alkalies and alkaline carbonates. It is less soluble in these fluids than is fibrinoplastin, and is not altered to the same degree by repeated precipitations and solutions as is the case with paraglobulin, which is rendered insoluble and inactive by four successive precipitations with sodic chloride. But, like fibrinoplastin, it is precipitated from its solutions by sodic chloride in excess.

IV. *The blood ferment* is prepared by mixing the blood serum of the ox with 15 to 20 times its volume of strong alcohol, and filtering from 15 days to a month, or better even 3 or 4 months, after. The precipitate contains coagulated albumen and the ferment. This is dried over sulphuric acid, then finely powdered, and rubbed up with water for at least ten minutes, using 65 c.c. of water for every gram of powder. Filter, and in the filtrate will be found the ferment; the filtrate is purified by treating it with carbonic anhydride and shaking it in the air so long as any opalescence shows itself. The ferment may also be extracted by digesting albuminous coagulum with glycerin.

The ferment may be more easily prepared by digesting washed bloodclot in an 8 per cent. solution of sodium chloride (GAMGEE).

This ferment is most active about blood heat.

v. *The plasmin of Denis* is a soluble substance existing in the blood plasma, and formed by the union in variable proportions of soluble and insoluble fibrin, as Denis terms them, the vital action of the vessels under normal conditions maintaining these constituents apart.

It is prepared by separating the corpuscles from the blood plasma by means of sodic sulphate, and adding crystals of sodium chloride to the plasma. A soft white mass is obtained by filtration, and if this is shaken in 10 to 20 times its weight of water it will dissolve, but at the end of 10 to 15 minutes it will separate as a coagulum.

All these bodies come most probably from the destruction of the pale corpuscles (Schmidt), though the red corpuscles no doubt also contribute. And it has been stated by Mantegazza that these pale corpusclus are the cause of coagulation, since when irritated by foreign bodies or inflamed tissues they set at liberty one or all of the generators of fibrin.

The Generation of Fibrin.—According to Schmidt this body results from the combination of the fibrinogen and fibrinoplastin that are present in the blood in unequal proportions, and remain separate till certain circumstances arise that bring about their union. But for this union to occur and coagulation be produced Schmidt states that there must also be present a ferment and a small quantity of salts, such as sodium chloride.

Hammarsten affirms, however, that the fibrinogen obtained from hydrocele fluid can be coagulated in the absence of fibrinoplastin when a little calcium chloride and blood ferment are added. So that according to him there is *only one generator* of fibrin—that is, fibrinogen. Frédéricq also states that the quantity of fibrin furnished by a solution of fibrinogen on the action of a ferment does not equal in weight the amount of precipitate given by the same solution when heated to 56°; and he has given proof that fibrinogen exists as such in living blood inside the vessels.

This evidence therefore seems in favor of there *being but one generator of fibrin*, viz. *fibrinogen*, which under favorable circumstances is decomposed or converted into fibrin, this conversion being apparently connected with the action of a ferment derivative of the pale corpuscles.

III. **FIBRIN.**—

100 parts give	C	52·6
	H	7·0
	N	16·6–17·4
	S	1·2– 1·6
	O	21·9–22·6

It yields 1·9 to 2·1 per cent. of ash, consisting of phosphate of lime and a little magnesic phosphate and sulphate, carbonate of lime, and iron.

About one-fourth per cent. can be obtained from normal blood.

Fibrin is a white, elastic, more or less fibrillated solid, insoluble in water and dilute solutions of sodium chloride; it swells much in dilute acids, but less so in dilute alkaline solutions, the material thus swollen being coagulable by heat and dissolving readily in a pepsin solution. Fresh fibrin dissolves more or less slowly at 35° to 40° in dilute solutions of potassic nitrate (1 : 17), and in 10 per cent. solutions of sodic chloride and sodic sulphate, as well as in dilute alkaline solutions generally—these solutions being coagulable by heat, and precipitable by acids, alcohol, and excess of sulphate of magnesia in powder. It is with difficulty soluble in dilute acids; in 1 to 5 per cent. solutions of hydrochloric acid it merely swells up, not being dissolved, but at a temperature of 40° to 60° the solution is rapidly effected, or after several days at ordinary temperatures. When dissolved in strong hydrochloric acid with the aid of heat it forms a violet-colored solution.

When boiled with caustic potash it evolves ammonia, and potassic sulphide is formed.

It decomposes hydric peroxide, so that if to oxygenated water a few drops of tincture of guaiacum are added, and then some fibrin that has been steeped in alcohol, a blue coloration is developed. Or the same coloration can often be more characteristically obtained by placing on a piece of filter paper, moistened with freshly prepared tincture of guaiacum, a little fragment of fibrin that has been immersed in a solution of hydric peroxide or ozonized turpentine.

Globulin, myosin, and fibrin form a series, myosin being intermediate in its characters between the other two. This is seen in their solubilities in dilute acids, alkalies, and neutral salts, fibrin being with difficulty soluble, myosin slightly soluble, and globulin on the other hand being easily soluble.

Preparation.—1. Fibrin is usually prepared by rapidly stirring freshly drawn blood with a bundle of twigs, and washing the filamentous coagulum with water, and then with alcohol and ether.

2. The fresh blood can also be well shaken in a bottle with several irregular pieces of lead, and the fibrin adhering to the lead detached and treated as in 1.

3. Cut some coagulated blood into small bits, enclose them in a linen cloth, and leave the mass under an open cold-water tap for several hours, the mass being squeezed from time to time and the washing continued till all traces of red coloration have been removed. The resulting white fibrin is then immersed in sodic chloride solution for 3 days to separate any globulin, subsequently for 14 days in distilled water that is changed from day to day, and finally digested with alcohol and ether.

IV. **ALBUMINATES** (*Derived Albumens*).—The native albumens are readily converted into one of these bodies by the gradual action of acids and alkalies, and the resulting compounds may be regarded respectively as acid and alkali combinations with the neutralization precipitate. The solid albuminates are insoluble in water and sodic chloride solutions; when freshly precipitated they are easily soluble in dilute acids, alkalies, and alkaline carbonates, and *their solutions are precipitated by careful neutralization, but not by boiling*, and only with difficulty by alcohol. Some of the acid albuminates contain sulphur, but the alkaline albuminates do not.

(*a*) **Alkali Albumen or Albuminate.**—This body is present in all young colorless cells, in blood corpuscles and blood serum, and in the chyle; also in muscle, pancreas, nerve, lens, and cornea.

It is possible that several forms of it exist, judging from the varying polarizing power of different alkali albuminates: thus when prepared from serum albumen by the action of strong caustic potash it is equal to —86°, from egg albumen it is equal to —47°, but if from coagulated egg albumen it rises to —58·8°.

Potash and soda dissolve albumens, transforming them, especially with the aid of heat, into alkali albumens.

Acids added to a solution of alkali albumen to exact neutralization precipitate pure albumen, but no precipitation occurs in presence of alkaline phosphates so long as there are not more than 9 molecules of acid phosphate to 1 of neutral phosphate, but the slightest excess of acid after this point will produce a precipitate.

A solution of alkali albuminate can be boiled without a precipitate occurring, but the addition of ether or alcohol, especially if the albuminate is concentrated, causes a turbidity. Salts of the heavy metals, baric chloride, and alum also produce precipitates.

A soda albumen resembling casein is present in the blood, and can be precipitated by acidifying the serum slightly with very dilute acetic acid after the fibrinoplastin has been separated by carbonic acid. This substance is most abundant in the blood of the spleen.

1. **Preparation of a Solid Alkali Albuminate.**—Remove the whites of two fresh eggs, divide the mass freely with scissors, and when it has been well shaken up in a flask filter through linen; then add strong caustic potash to the filtrate until it becomes a firm jelly. This is to be cut into bits, rolled up in a piece of gauze, and washed well in distilled water.

This albuminate is soluble in boiling water, from which it is precipitated by the careful addition of acetic acid.

2. Dilute the white of egg (prepared as before) with an equal volume of water, filter, and evaporate to half its bulk; when it has cooled add caustic potash drop by drop until it becomes gelatinous. This mass is cut into bits, as already described, well washed in a large excess of distilled water, rapidly strained through a linen cloth, and again washed there with more water until the alkaline reaction has quite disappeared. This washing must be done rapidly, and the purified albumen thus obtained dissolved in boiling water and precipitated therefrom with acetic acid (after Lieberkühn).

3. Shake milk with strong caustic soda and with ether, decant the ether, precipitate the albumen with acetic acid, and wash it with water, cold alcohol, and ether (Hoppe Seyler).

(β) **Casein** is present in the milk of all animals, and a somewhat similar body is also described as existing in blood serum, chyle, muscle juice, and serous exudations.

In the milk casein exists chiefly in the soluble form, in combination with an alkali, and some say combined with calcic phosphate; accordingly, when this latter body is removed from its combination with the casein by the action of an acid, the casein is precipitated; but a small quantity is present also in an insoluble condition in some saline combination (Commaille). It is yet difficult, notwithstanding, to say positively how much of the casein is in the soluble form and how much is only suspended in a finely granular form.

Casein resembles an alkali albumen, but it is somewhat richer in nitrogen; heated also with caustic potash it yields sulphur, potassium sulphide being formed, which is not the case with with an alkali albumen; further, casein differs from an alkali albuminate in its inability to pass through a filter and in being coagulated by rennet.

Its solutions do not coagulate when heated; they are precipitated by acetic and most acids, being soluble in excess; but no precipitation occurs on simple neutralization in presence of potassic phosphate, although it will take place when a sufficient excess of acid has been added.

Rennet also, which contains a special ferment, can precipitate casein even from an alkaline milk at a moderately elevated temperature, 1 gram sufficing to coagulate 30 litres of milk. Casein is likewise separated from its solutions by boiling them with calcic chloride or magnesic sulphate. A solution of casein in acetic acid is precipitated by dilute sulphuric acid and by potassic ferro- and ferri-cyanide.

The specific rotatory power of a casein solution for yellow light varies from 76° to 91°, according to the alkalinity of the solvent, being higher when a strong instead of a weak alkali has been employed; a solution in dilute hydrochloric acid has a rotatory power equal to —87°.

A conversion of casein into fat occurs when milk is allowed to stand for some time.

While the identity of soluble casein and sodic albuminate is maintained by most German chemists, the question cannot yet be regarded as decided. Opinions vary; Danilewski and Badenhausen, for example, affirm that casein is a mixture of two substances, one of which is an albumen probably identical with serum albumen, and the other protalbin, a transition product formed during the peptonization of various albumens with alkalies and pancreatin. It is this protalbin, they say, that imparts to casein its acid character.

Casein of woman's milk is slightly different from that of cow's milk, being only partially precipitated by acetic acid and carbonic acids, and appearing in grayish white flocculi instead of in lumps.

There is a slight difference also in their percentage composition.

Casein.	(Woman.)	(Cow.)
C	52·35	53·62
H	7·27	7·42
N	14·65	14·20
O	25·73	24·76 (Makris.)

The casein of cow's milk is also more soluble in water and alcohol than the casein of woman's milk.

To separate casein from skimmed milk, dilute the latter with 10 times its volume of water, and add a few drops of dilute hydrochloric or acetic acid until a precipitation begins to occur; now pass a current of carbonic acid, filter, and wash the coagulum with cold water, and afterwards with alcohol and ether; or, to render it purer, after the cold water wash it with water acidulated with hydrochloric acid, and subsequently with pure water. Now heat to 45° with a large volume of water, when it will in great part dissolve; filter, and precipitate the dissolved casein with carbonate of ammonia. Collect the precipitate and wash it with water, and then with warm spirits and ether.

With human milk it is better to precipitate the casein with sulphate of magnesia added to saturation to the milk warmed to 30°, to wash the separated casein with a saturated solution of this salt, and then with alcohol and ether. To purify it redissolve in water, and dialyse to separate the magnesic sulphate completely.

A nearly pure solution of casein is also obtained by dialysing milk 30 to 36 hours (SCHMIDT).

(γ) **Acid Albuminate** (*Syntonin*, *Albumose*).—The majority of acids in the dilute condition and at ordinary temperatures transform albumens into acid albumen, which is also the first product of the action of gastric juice on proteids. The conversion is accelerated by raising the temperature. The term acid albumen has generally been applied to the combination with acetic acid alone (but this, we see, is incorrect), and *syntonin* to the combination with hydrochloric acid, especially when myosin has been employed. This is the percentage composition of the syntonin: C 54·1, H 7·3, N 16·1, O 21·5, S 1·1.

An acid albuminate is a white gelatinous substance insoluble in water and sodic chloride solutions, but easily soluble without alteration in very dilute hydrochloric acid and dilute caustic alkalies. Its solutions have a specific rotatory power for yellow light of—72°, which rises to —84·8° when the solution is heated in a closed vessel.

Acid albumen solutions are precipitated by neutralization even in presence of sodic or potassic phosphate, also by saturating them with sodic chloride, acetate, or phosphate; but they are not affected by boiling. *The solution in lime water is, however, partially coagulated by boiling, and a still further precipitation occurs after boiling on the addition of sodium chloride or magnesium sulphate.* Indeed, a precipitate is generally produced on boiling an alkaline solution of any acid albumen to which magnesic sulphate has been added in excess.

Preparation.—Digest egg albumen or dissolve serum albumen in fuming hydrochloric acid, and let it stand till the solution is blue-colored; then dilute with twice its volume of water. Collect the precipitate, dissolve it in water, and carefully neutralize the solution with sodic carbonate; finally wash well with water.

To *prepare syntonin*, finely divided muscle as free from fat as possible is well washed and placed in one-fifth per cent. hydrochloric acid, which dissolves it readily; the solution is filtered after a few hours, and the opaline, slightly viscid filtrate diluted and exactly saturated with sodic carbonate: gelatinous flakes are obtained, which are to be washed in water.

Tests.—1. A solution on boiling remains clear; then acidify strongly with acetic acid and add a saturated solution of sodic chloride until a precipitate appears. On heating the precipitate disappears; now add more sodium chloride, and a point will soon be reached when boiling will no longer clear up the mixture, and the albumen will be completely precipitated by the sodium chloride.

2. Pure nitric acid gives a precipitate which dissolves with an intense yellow color on heating.

3. Add caustic soda, and then a drop or two of a weak solution of cupric sulphate; an intense purple violet color is produced.

4. With Millon's reagent a deep red color is given on heating, but the presence of much sodium chloride interferes with the reaction.

5. To separate this body from fluids containing it, boil them with hydrated oxide of lead (HOFMEISTER).

V. **PEPTONES.**—The gastric juice converts albuminous bodies into peptones; pancreatic juice likewise possesses the same property, and possibly also the intestinal juice, but to a limited degree. All proteids, in short, except amyloid substance yield peptones with acid gastric or alkaline pancreatic juice at the temperature of the body. It is said, further, that they are produced by the prolonged action of dilute acids at high and of moderately strong acids at medium temperatures, also by the action of water at very high temperatures and pressures. In all these cases it is probable that an albuminate is first formed.

All proteids are also said to be converted into peptone by prolonged contact with animal and vegetable tissues, the conversion of swollen fibrin into peptone by the action of the tissue of the lungs or kidneys taking place as energetically as under the influence of pepsin (EICHWALD, POEHL), and it is well known that the juice of the so-called carnivorous plants (*drosera*, etc.) when acidified with hydrochloric acid (one-fifth per cent.) dissolves fibrin as rapidly as does pepsin itself.

In the decomposition of albumens by bacteria peptone is also one of the early products.

Peptone has been found in the liver and spleen in leukæmia, and in certain pathological urines it is occasionally present.

The peptones are said to possess a slightly different composition from the albumens from which they were derived in containing a smaller proportion of carbon and nitrogen. They seem to result from the fixation of a certain quantity of water with the albuminous matters. MALY, however, regards the peptones as possessing the same elementary composition as their derivative albumens. In the subjoined table three analyses of fibrin are given, and three of fibrin peptone:—

	Fibrin.			Peptone.		
	MUNK.		KISTIAKOWSKI.		KOSSEL.	MALY.
C	51·40	52·51	52·32	46·67	48·97	51·40
H	6·95	6·98	7·07	7·12	7·06	6·95
N	17·13	17·34	16·23	16·30	15·14	17·13
S	1·13	1·18	1·35	0·93	1·16	—
O	—	—	23·03	28·98	27·67	—

Peptones have also been regarded as due to the swelling up of the colloid of albumen, the inner constituent remaining the same, no change in specific gravity, rotatory power, or index of refraction taking place in the conversion (POEHL).

But the proportion of salts in peptone is undoubtedly smaller than that of the albumen from which it was derived; thus in serum albumen the salts are = 9·6 per cent., in egg albumen = 5·43 per cent., in fibrin = 2·17 per cent., but in peptone only = 1·16 per cent. By the digestion of fibrin MÖHLENFELD obtained a peptone having the composition $C_{143}H_{301}N_{40}SO_{62}$. It is evident, therefore, that at present we cannot say that any constant difference has been conclusively established, although there is a slight probability in regarding peptones as hydrates of albumen.

Different peptones have been described, but those given by MEISSNER cannot all be regarded as true peptones. KÜHNE distinguishes *hemipeptones* and *antipeptones*, the former being readily capable of conversion into leucin and tyrosin under the action of trypsin, while antipeptones resist this decomposition.

Between the genuine proteids and the peptones there exist gradual states of transition, depending only on different states of hydration, a peptone being capable of reconversion into precipitable albumen by treatment with dehydrating agents, such as alcohol and salts of the alkalies; and by heating a peptone for some hours to 130°–140° it changes more or less completely into albumen (HENNINGER).

Preparation.—1. Some freshly prepared fibrin is to be cut up very fine and covered with 5 or 6 times its volume of hydrochloric acid (one-fifth per cent.) As soon as the fibrin has assumed a transparent aspect add a little glycerine solution of pepsin, and warm the whole up to 40° over a water bath. After several hours the gelatinous mass will have disappeared, and an opalescent gray solution taken its place; strain, and render the filtrate faintly alkaline with sodic carbonate. When the resulting precipitate has settled, filter; boil the filtrate after having acidified slightly, and filter afresh. From this last filtrate the peptone is precipitated with absolute alcohol, the collected precipitate extracted with ether and a mixture of ether and alcohol, and the residue covered with absolute alcohol for 2 or 3 weeks. The white mass is then filtered from the alcohol and dissolved in a little water at a gentle heat; the filtrate is precipitated with absolute alcohol, and the precipitate dried at 30° *in vacuo* (ADAMKIEWICZ).

2. Digest the finely divided mucous membrane of a pig's stomach for some time with one litre of water and 10 c.c. hydrochloric acid, or add the glycerin extract of the same mucous membrane to the same volume of water and acid. Now place a little well-washed fibrin in some of the above digestive fluid, and leave it aside at a temperature of 40° for 2 or 3 days; then neutralize with carbonate of soda, warm gently, and filter; concentrate the filtrate slightly by evaporation, and dialyse it until no more chloride passes through; concentrate still further, and precipitate with absolute alcohol; after some time collect on a filter, wash with alcohol and ether, and dry *in vacuo* (MALY).

Properties and Specific Characters.—Peptones possess in a feeble degree the character of acids; yet they appear also to form combinations with acids. The solid peptones are amorphous, yellowish white, somewhat translucent, inodorous, and hygroscopic powders, that are very soluble in water, particularly when warmed, and to a less extent in dilute alcohol, while they are insoluble in absolute alcohol, ether, and chloroform.

1. Like albumose and albumen, peptones in neutral or weakly acid solution are precipitated by mercuric chloride, mercuric nitrate, silver nitrate, the lead acetates, tannic, picric, and the biliary acids; also by alcohol, but to a less extent and with difficulty; and by phosphomolybdic and phospho-tungstic acid.

2. Unlike albumen and albumose, they are not precipitated by heat and mineral acids, nor by acetic acid and potassic ferrocyanide, cupric sulphate, ferric chloride, or sodium chloride, nor by neutralization of their acid or alkaline solutions.

3. Their solutions diffuse readily through animal membranes, but their osmotic power is comparatively feeble; in this respect, however,

they differ from all other proteids, which diffuse with the greatest difficulty, or not at all.

4. They give the protein reactions, but with strong caustic soda and a mere trace of a dilute cupric sulphate solution, an intense *purple-or rosy-red, pinkish, or reddish violet coloration*—the so-called biuret reaction—appears instead of a blue or violet color. Albumose gives the same, and albumen only a blue, but in no case a red or pink coloration.

5. Like the albumens generally they polarize to the left, the degree of polarization not, however, being affected by heat, but albumen (of egg) peptone polarizes more powerfully than fibrin peptone.

6. Peptones and acid albuminates are thus distinguished:—

Peptones.	*Acid Albuminates.*
The aqueous solutions, when slightly acidified, are not precipitated on being exactly neutralized or heated.	The slightly acid aqueous solution is precipitated when exactly neutralized.
Acids produce no precipitation or other disturbance.	Most of the acids, including acetic, give a precipitate soluble in excess.
The metallic salts, with the exception of those of mercury, give no precipitate.	These salts give slight precipitates, but some of them are soluble in excess.
Assimilable and dialysable.	Not directly assimilable, and dialyse with difficulty.

VI. **AMYLOID SUBSTANCE, LARDACEIN.**—This is an amorphous, friable, white substance that appears to be a fibrin derivative. It has this percentage composition: C 53·6, H 7·0, N 15·5, O 22·5, S 1·3, and only occurs as a pathological product. It is generally found in the form of little transparent grains or corpuscles, or as fine granulations with concentric layers, as in the brain and prostate, or as an infiltration in the liver, spleen, kidneys, and walls of blood vessels.

Lardacein is insoluble in water, alcohol, ether, dilute acids, and the alkaline carbonates; it neither swells in saline solutions nor is it digested by gastric juice at the normal temperature of the body; it is soluble in strong hydrochloric acid, the solution when diluted with water precipitating syntonin, and when boiled with dilute sulphuric acid (1:6) it dissolves with a violet color, and with strong sulphuric acid furnishing leucin and tyrosin; the alkalies dissolve it, transforming it into a substance analogous to albuminose.

Tests and Characteristics.—1. Amyloid substance gives a *reddish brown coloration* with iodine, not a yellow stain, as with ordinary albumen; with *iodized chloride of zinc* it gives a more marked red coloration; and if a little *iodine solution* is first added to it, and then a little *sulphuric acid, a violet or blue coloration* appears. When this last test is applied to an affected organ, as in the *post-mortem* room, the blue obtained is dark and dirty-looking, not the bright clear blue given by the purified lardacein.

2. *Anilin violet, or methyl anilin*, is particularly useful for the identification and demonstration of this degeneration: healthy tissues are stained by it of a violet or blue, but the parts that have undergone amyloid degeneration take a rosy red or reddish violet color. This test

is chiefly applicable to the staining of sections for microscopic examination. A dilute watery solution of the violet of Paris gives good results, and a few minutes' immersion are sufficient to effect the necessary staining. Or a strong watery solution may be made and the section deeply stained therein; it is then to be washed in acetic acid (1 to 2 per cent.) until all excess of color has been removed.

3. *Eosin* stains it a bright red, and this reagent is also applicable to microscopic examination.

4. A solution of the body in strong sulphuric acid gives a purple violet color with sugar or acetic acid. Purified lardacein also dissolves readily in dilute ammonia, and when excess of ammonia has been driven off the neutral solution gives precipitates with dilute acids.

5. It also gives the xanthoproteic reaction, and the red coloration with Millon's reagent.

To extract it from an affected organ, cut the latter in pieces, remove the vessels as far as possible, wash in cold water, and boil; treat the residue with alcohol and ether; next boil repeatedly with alcohol acidulated with hydrochloric acid, and then digest with excess of gastric juice at 40° so long as the filtrate gives the xanthoproteic or a peptone reaction. Boil the insoluble residue once more in spirit containing hydrochloric acid, and then wash thoroughly with water. Amyloid substance remains behind.

VII. **COAGULATED ALBUMEN.**—This, as we have already seen, is produced by the action of heat on solutions of egg and serum albumen, or on such albumens as the globulins or fibrin when suspended in water or dissolved in saline solutions; also by the prolonged action of absolute alcohol on the same bodies.

It is insoluble in water, dilute acids and alkalies, and neutral saline solutions; but it is soluble in strong acids and alkalies, and even in dilute acids and alkalies at elevated temperatures, in both cases forming albuminates; further it is easily converted into peptone by the gastric or pancreatic juices at the blood heat, and is colored yellow by iodine.

VIII. Two special forms of albumen, **METALBUMIN** and **PARALBUMIN**, will here be referred to, although their true constitution is not yet accurately known and the accounts given of them are somewhat conflicting. They were first found in ovarian cysts and ascitic fluid. They are thready and of a slimy consistency only imperfectly precipitated by boiling, and their precipitates with alcohol are soluble in water.

(*a*) **Metalbumin** has been regarded by some writers merely as a mixture of albumen and mucin. It has been found in ascitic fluid and in certain serosities.

1. Its solutions are not precipitated by acetic or hydrochloric acid, or by acetic acid and potassic ferrocyanide, and boiling merely renders the solution cloudy without coagulating it, and by alcohol it is precipitated but not coagulated.

2. It is abundantly precipitated by mercuric chloride and by tincture of nut galls.

(*β*) **Paralbumin.**—It is doubtful also whether this body is a true proteid; it generally appears to be associated with some glycogen-like substance. HAERLIN assigns it this percentage composition: C 51·8, H 6·9, N 12·8, S 1·7, O 26·8. It has been met with in the fluid of ovarian cysts, of which it used to be regarded as characteristic, but it has likewise been met with elsewhere. Its alkaline solutions are very ropy. Peculiar pear-shaped cells (SPENCER WELLS) are described as present in the fluid in which it is found, and also granular cells somewhat resembling those of pus; but the granular appearance of these cells is not removed by acetic acid, and under treatment with ether the granules become more transparent (DRYSDALE).

1. In aqueous solution it is precipitated by alcohol, but the precipitate dissolves in excess of water at 35° at the end of a few hours.

2. Boiling precipitates it imperfectly, causing only an opalescence or turbidity, which disappears on the addition of strong acetic acid, although flocculi may sometimes show themselves.

3. Acetic acid produces a turbidity which dissolves in excess of acid or in a strong solution of sodic chloride, in this respect differing from the acetic acid precipitate with mucin, which is insoluble in excess of the precipitant or in sodic chloride solution.

4. Carbonic acid gas passed through a diluted solution gives a flocculent precipitate.

5. Abundant precipitates are also given by nitric acid, ferrocyanide of potassium and acetic acid, hydrochloric acid, mercuric chloride, basic acetate of lead, and tincture of nut galls.

CHAPTER XIX.

TABLE IDENTIFYING THE CHIEF DIFFERENT FORMS OF ALBUMEN.

I. *Soluble in Pure Water.*

A. Coagulated by heat, and not precipitated by carbonic acid.
  Native albumens.
    1. *Serum albumen*, not precipitated by ether.
    2. *Egg albumen*, precipitated by ether.

B. Not coagulated by heat.
  Peptones.—Not precipitated by sodic chloride, acids, or alkalies, nor coagulated by long exposure to alcohol; give a *rose color* with a trace of cupric sulphate and much caustic soda.

II. *Insoluble in Pure Water, but Soluble in Dilute Solutions of Sodium Chloride* (1 per cent.)

Globulins.—Coagulated by heat, precipitated by carbonic acid, and easily convertible into derived albumens.

A. Precipitated by saturation with sodium chloride.
  (*α*) Coagulated by fibrin ferment.
    1. *Fibrinogen.*
  (*β*) Not coagulated by fibrin ferment.
    2. *Fibrinoplastin.*—Precipitated by saturation with magnesium sulphate; forms fibrin with fibrinogen and ferment.
    3. *Myosin.* Does not form fibrin with fibrinogen.

B. Not precipitated by saturation with sodium chloride.
    4. *Vitellin.*
    5. *Crystallin.*

III. *Insoluble in Pure Water or Dilute Sodium Chloride, but Soluble in Acids or Gastric Juice.*

A. Soluble in dilute hydrochloric acid or dilute alkalies.

(*a*) *Derived albumens* or *albuminates* (soluble in the dilute acid —one-tenth per cent.—in the cold).

1. Precipitated by neutralization in presence of alkaline phosphates.

Acid Albumen.—Precipitated by saturation with sodium chloride, insoluble in hot spirit.

2. Not precipitated by neutralization in presence of alkaline phosphates.

Alkali Albumen.—Treated with strong caustic potash, potassium sulphide not formed; soluble in hot spirit; not coagulable by rennet.

Casein.—Heated with caustic potash, potassic sulphide is formed. Is coagulated by rennet.

(*β*) *Fibrin.*—[To dissolve in dilute hydrochloric acid (one-tenth per cent.) it requires to be heated for several hours up to 40° or 60°.]

Not soluble in one-tenth per cent. hydrochloric acid in the cold, this only causing it to swell up, but readily dissolved on the addition of a little pepsin.

Gives a blue coloration with freshly-prepared tincture of guaiacum and hydric peroxide.

B. Insoluble in dilute acids and alkalies, but easily soluble when digested with gastric or pancreatic juice, forming peptones.

Coagulated Albumen.—The protein reactions are easily obtained with the dry solid.

C. Insoluble in water, sodium chloride, dilute acids, or gastric juice; soluble in the stronger alkalies and in strong hydrochloric acid.

Amyloid Substance.—Gives a reddish color with iodine, a blue with iodine and sulphuric acid, and a rosy red with methyl violet.

CHAPTER XX.

THE COLLAGENS.

THESE bodies are closely allied to the albumens, but when treated with acids or dilute bases they do not, like them, yield syntonin. Ossein and gelatin are types. They are poorer in carbon but mostly richer in nitrogen than the albuminoids. A common property possessed by them is that of their *hot aqueous solutions solidifying into jellies on cooling.*

The alimentary value of gelatinous bodies is still involved in some uncertainty. They are stated by MAJENDIE and others to have no alimentary value, but others again are of opinion that they possess real nutritive properties, to some extent forming a substitute for other plastic material, and, therefore, by their admixture with the food, admitting without disadvantage of a diminution in the proteids (BISCHOFF and VOIT). Even elastin, it is now stated, is dissolved by the gastric juice, furnishing peptone (ETZINGER, HORBACZEWSKI).

Percentage composition.	C.	H.	N.	O.	S.	Authority.
Ossein	49·9	7·3	17·2	24·9	0·7	FREMY and VERDEIL.
Gelatin	50·0	6·5	17·5	25·4	0·6	FREMY and SCLIEPER.
Chondrin . . .	49·3	6·6	14·4	29·3	0·4	MULDER.
	47·7	6·7	13·8	31·0	0·6	LANDWEHR.
Mucin	52·2	7·0	12·6	28·2	—	HOPPE SEYLER.
Elastin	55·5	7·4	16·7	20·4	—	HOPPE SEYLER.
	54·3	6·9	16·7	21·4	—	HORBACZEWSKI.

The chief collagens are *ossein*, *gelatin*, and *chondrin;* an allied body is *mucin*, and accordingly for convenience sake it will be described at the same time, as also elastin.

I. **GELATIN** (*Glutin*).—When some dried and purified powdered bone is digested with dilute hydrochloric acid (10 per cent.), the earthy salts will be slowly removed and the body called *ossein* will remain behind. Dry bones yield 29 to 30 per cent. of this body. It is insoluble in water, hot or cold, but when heated in a Papin's digester it is dissolved and yields gelatin; indeed, ossein and gelatin have almost the same composition, and by boiling ossein with water it is very rapidly and completely changed into gelatin. It does not, however, yield glucose when boiled with acidulated water.

Collagen is the name given to the substance of which white fibrous connective tissue consists, although it is not present in their embryonic condition. The action of boiling water converts it into gelatin. After 30 hours' boiling collagen no longer gelatinizes, but is resolved into two peptones, one insoluble in alcohol and precipitated by platinic chloride (*semiglutin*), the other soluble in alcohol but precipitated by the platinum salt (*hemicollin*)—$C_{102}H_{149}N_{31}O_{38}$ (*collagen*) = $C_{55}H_{88}N_{17}O_{22}$ (*semiglutin*) + $C_{47}H_{70}N_{14}O_{19}$ (*hemicollin*) (HOFMEISTER).

To **prepare the collagen** pieces of tendon are sliced thin. soaked for some time in cold water. then for several days in weak lime or baryta water; afterwards washed in water. then in very dilute acetic acid. and again in water. The residue thus obtained is collagen mixed with some elastic tissue.

The collagen and ossein appear to be closely allied, if not identical.

Long-continued boiling of white fibrous tissue, skin, or bone yields, as we have seen, a watery solution of gelatin. Gelatin is later in its appearance than either mucin or chondrin, for, while certain embryonic tissues yield mucin and chondrin on boiling, they give no gelatin, though this replaces them when these tissues have undergone development.

Pure gelatin is prepared from commercial gelatin by soaking the latter several days in distilled water, which is changed from time to time. It will then have swollen up considerably. and is next to be dissolved in distilled water with the aid of heat. After the solution has stood some time. to allow any sediment present to fall, it is filtered hot into 90 per cent. alcohol, when the gelatin will separate in thready masses. These are to be collected, cut fine, and dried, first in the air and then over a water bath.

It is also readily prepared by dissolving isinglass in dilute hydrochloric acid, and dialysing the solution.

Properties.—In the pure state gelatin is slightly yellowish or almost colorless, transparent, vitreous, and tasteless; it swells in cold water without dissolving, but is readily soluble in hot water or hot glycerin, the solution *setting* or gelatinizing on cooling, even one-tenth per cent. solutions possessing this property; but long-continued boiling, either alone or after the addition of a little nitric or acetic acid, or heating up to 140° in a sealed tube, destroys this power of setting. Gelatin is soluble in dilute acetic or other acids, but is insoluble in oils, alcohol, and ether. Its watery solutions polarize to the left (about 130° at 30°).

Solutions of gelatin take up more calcic phosphate than does pure water. Its alkaline solutions dissolve cupric oxide with a violet color, which on long boiling becomes yellowish red, but without any separation of reduced oxide, as this is soluble in alkaline gelatin solutions: its presence, therefore, interferes with Trommer's test for sugar.

In the direct sunlight gelatin combines with potassic chromate, forming a yellow, insoluble, amorphous mass.

Derivatives.—As the result of putrefaction gelatin is decomposed, and among the products we have a little leucin and much glycocin, ammonia and some of the fatty acids also being present, but no tyrosin.

When 1 part of gelatin is boiled with 4 parts of sulphuric acid and 12 parts of water for 36 hours, excess of milk of lime or baryta then added, the whole boiled and filtered, the filtrate acidified with sulphuric acid, again filtered and evaporated to a small bulk, granular crystals of *glycocin* or *amido-acetic acid* ($C_2H_5NO_2$) will be obtained. These form rhombic transparent prisms that possess a sweetish taste and are insoluble in alcohol and ether. By the prolonged action of hydrochloric acid at 38°, or of acid pepsin, a gelatin peptone is obtained which is diffusible but no longer gelatinizes.

Further, if boiled some hours with *strong caustic potash*, then neutralized with sulphuric acid, evaporated to a small bulk, and the residue extracted with hot alcohol, *leucin* will be obtained on evaporating the alcohol.

Tests.—1. Gelatin solutions are precipitated by mercuric and platinic chlorides, tannic acid, alcohol, and chlorine water, the precipitates being more or less viscid and slimy, separating imperfectly, and insoluble in alcohol, ether, and water, but soluble in the alkalies. With the mercuric chloride and tannic acid the precipitates are insoluble.

2. Gelatin is not precipitated from its watery solutions by acids, acetate of lead, or by alum.

3. By its property of gelatinizing it is possible to identify gelatin if its solution is not too dilute.

4. Gelatin is distinguished from a proteid by giving no precipitate with acetic acid and potassic ferrocyanide, or with most metallic salts; and from chondrin by not being precipitated by acetic acid. Watery solutions polarize to the left to a less extent than solutions of chondrin.

II. **CHONDRIN.**—When the permanent cartilages are boiled chondrin is obtained as the product; it is derived from the intercellular substance and the capsules, but not from the cells themselves. A somewhat similar body is obtained by boiling the cornea. The name **chondrogen** is given to the material of which this intercellular substance is composed, just as the name *collagen* is applied to the constituent principle of white fibrous tissue which yields gelatin on boiling.

Preparation.—Boil some costal cartilage for about half an hour, then detach the perichondrium and cut the cartilage into as small pieces as possible, which are to be macerated some hours in cold water and then heated up to 120° for two or three hours in a Papin's digester under a pressure of two or three atmospheres, or boiled instead for 24 to 48 hours or so at ordinary pressures. Filter the hot extract rapidly, evaporate the filtrate, and after treating the residue with cold water dry and reduce it to powder, and having boiled it with alcohol dry it again. Or acetic acid can be added to the filtrate, and the precipitated chondrin can be exhausted with alcohol and ether, and then dried (HOPPE SEYLER).

Properties.—Dry chondrin forms a hard, translucent, yellowish mass, insoluble in alcohol and ether, swelling up in cold, but dissolving in hot water and alkaline solutions. Like gelatin the solution of chondrin in hot water sets when the solution cools, but by prolonged ebullition, or by treatment with alkalies, solutions of both bodies lose this property. A watery or alkaline solution has a polarizing power = —213·5°, but as high as —552° with excess of alkali (HOPPE SEYLER).

Derivatives.—Chondrin is closely allied in its characters to gelatin, as they both, when decomposed by boiling with baric hydrate, give the same products, except that chondrin yields three times as much acetic acid as gelatin; but when decomposed with sulphuric acid chondrin only yields leucin and little or no tyrosin and glycocin. Chondrin also, on being boiled a long time with hydrochloric or sulphuric acids, or when digested with gastric juice, furnishes a substance resembling an acid albumen, as well as a nitrogenous body (chondroglucose) capable of reducing cupric sulphate in alkaline solutions, crystallizing and fermenting, however, with difficulty, and polarizing to the left (BÖDECKER); accordingly it may be regarded as a nitrogen-holding glucoside. In this respect mucin resembles chondrin.

Chondrin can be changed into gelatin under the influence of oxidizing agents (BRAME); and in the organism a similar change occurs, as when cartilage, yielding chondrin, gives place to bone, yielding gelatin. But chondrin is something more than 3 per cent. poorer in nitrogen than gelatin. In spite, however, of these points of difference there seems some probability in MOROCHOWITZ's opinion that chondrin and gelatin are identical, chondrin only differing from gelatin in being a mixture of this body with mucin and salts.

Characteristics and Tests.—1. Chondrin as well as gelatin are distinguished from albumen in that their solutions in acetic or phosphoric acids are not precipitated by potassic ferrocyanide, and they are both precipitated by alcohol and chlorine water.

2. *Dilute mineral acids* precipitate it readily, but the precipitates are readily soluble in excess.

3. *The Organic Acids.*—*Acetic acid* gives a white precipitate, which is insoluble except in a very large excess; but the precipitate does not occur in presence of neutral salts of the alkalies or alkaline earths, and sometimes not with impure solutions.

Tartaric, *citric*, and *oxalic* acids have the same action, but the oxalic acid precipitate is soluble in excess.

Tannic acid gives no precipitate, only an opalescence.

4. *The salts of most of the heavy metals, as lead, copper, silver, and iron*, give precipitates that are wholly or partly soluble in excess. The lead precipitate is insoluble in excess, and no precipitate, but only an opalescence is given with mercuric chloride.

5. *Alum*, which gives no precipitate with gelatin, precipitates chondrin, but the precipitate disappears on the addition of excess of alum.

III. **MUCIN.**—This body is contained in the cement substance of the connective tissues, but it is specially abundant in the embryonic condition of these tissues and in the jelly-like variety; it is met with also in the cement between the cells of the epidermis, and is likewise one of the excretion products of the protoplasm of the epithelial cells lining mucous surfaces, and of the secreting mucous cells of the submaxillary and sublingual glands; it is further largely present in the bile.

Its structure is unknown, and the composition assigned to it varies, but, according to EICHWALD and SCHERER, its average percentage composition may be taken as C=49·5, H=6·7, N=9·6, O=34·2. Dry mucin yields about 2·44 per cent. of ash, and contains no sulphur.

Mucin is a nitrogenous glucoside, and it is probably an albumen derivative. HOPPE SEYLER, indeed, now classifies it with the albumens.

Preparation.—1. Cut the *submaxillary glands* of an ox into small pieces, and after washing these in a little water digest them for some time in water, then filter and precipitate the mucin in the filtrate with acetic acid; collect on a filter and wash thoroughly with water; next dissolve the precipitate with milk of lime, filter, and add acetic acid; the mucin thus precipitated is to be washed with water, and then with alcohol and ether in succession.

Or the cleaned glands are minced and rubbed up with powdered glass, the mass covered with water and filtered after 12 hours, and the extraction repeated. The filtrate is precipitated with excess of acetic acid, the separated mucin washed with water and a little acetic acid, then with warm alcohol, and finally dried (OBOLENSKY).

2. Digest finely-divided *tendon* with distilled water, and then with large quantities of lime or baryta water, from which the mucin is subsequently precipitated by acetic acid; filter and wash the precipitate with water and dilute spirit (ROLLETT).

3. *To extract mucin from bile* add to the bile its own volume of spirit (85 per cent.); the mucin is precipitated; separate it by decantation and wash with more spirit. Dissolve up the mucin in lime or baryta water, filter after some time, and reprecipitate by excess of acetic acid; collect on a filter, and wash it there with water, alcohol, and ether.

Properties.—Mucin generally presents itself in white or yellow thready and tenacious masses. It swells up in water without dissolving, but being readily miscible with it; if boiled with the water, however, for some time, a little of the mucin enters into imperfect solution. It is soluble in dilute hydrochloric acid (5 per cent.), in pancreatic juice, and in weak alkaline solutions, but insoluble in alcohol, ether, chloroform, dilute acetic acid, very dilute mineral acids (1 per cent. hydrochloric), or gastric juice. Acetic acid causes it to shrink, and caustic potash renders it at first more thready and then dissolves it.

Its neutral solutions are not coagulated by heat, and to these solutions it communicates a certain degree of viscosity, even when present in small amount.

Its solutions are precipitated by alcohol, alum, basic acetate of lead, acetic acid, and the dilute mineral acids, being soluble, however, in excess of the last; they are not precipitated by cupric sulphate, mercuric chloride, or potassic ferrocyanide, but when the last salt is added to a boiled solution of the mucin in glacial acetic acid a white precipitate is formed.

Mucin gives a rosy red coloration with Millon's reagent, and a yellow color with nitric acid. Like grape sugar its presence renders the precipitate given by the caustic alkalies with cupric sulphate soluble in excess, but leads to no change of color on boiling the solution.

Derivatives.—Mucin is decomposed when boiled with a dilute mineral acid like sulphuric into an acid albuminoid material and a body like sugar in its reducing powers, but not fermentable (Eichwald). When boiled for a considerable time with sulphuric acid diluted with its own weight of water, leucin and tyrosin are obtained in abundance, as well as about 7 per cent. of the compound ammonias (Städeler). Eichwald's mucin peptone is obtained by dissolving mucin in excess of lime water, boiling the solution until it gives no precipitate with acetic acid, then passing a current of carbonic acid gas through the solution, filtering, evaporating the filtrate to a small bulk, and precipitating with alcohol.

In the annexed table gelatin, chondrin, and mucin are compared.

	Gelatin.	Chondrin.	Mucin.
1. *Acetic acid* . .	Gives no precipitate, but dissolves in the acid; is precipitated from its solution when warmed with the alkaline salts.	A precipitate soluble in solutions of the alkaline salts.	A precipitate not soluble in solutions of the alkaline salts.
2. *Mineral acids* .	No precipitate.	A precipitate soluble in excess and in neutral saline and alkaline solutions.	A precipitate soluble in excess.
3. *Tannic acid* . .	A yellowish precipitate.	Only an opalescence.	—
4. *Acetate of lead* .	No precipitate.	A heavy precipitate, partly soluble in excess.	Precipitated by basic acetate of lead.
5. *Alum*	No precipitate.	A precipitate soluble in excess.	A precipitate.
6. *Mercuric chloride*	An abundant white precipitate.	No precipitate, only an opalescence.	Only a slight turbidity.
7. When decomposed by boiling dilute acids.	Leucin and glycocin formed; no sugar.	Leucin, but no glycocin formed; also chondroglucose.	Leucin and tyrosin and a body like chondroglucose make their appearance.

Pathology.—In certain abnormal affections included under the term *myxœdema*, there is generally observed a jelly-like swelling of the connective tissue due in part to an increase in its cement substance (ORD).

To obtain this mucin, mince the skin finely and digest with water for several days, filter, and precipitate the filtrate with excess of acetic acid; separate the precipitate after several hours have elapsed, then dissolve it in lime or baryta water, and after twenty-four hours reprecipitate with acetic acid. The precipitate thus obtained is to be washed with water, alcohol, and ether, and subsequently dried.

It is sometimes an advantage to immerse the skin in methylated spirit for several days, and then to digest at once in baryta water.

IV. **ELASTICIN** or **ELASTIN** is the name given to the substance composing the fibres of yellow elastic tissue. Although it is very closely related to keratin it will be described here for the sake of convenience.

To prepare it cut the ligamentum nuchæ of a giraffe, horse, or ox into thin pieces, and exhaust them successively with ether, hot alcohol, boiling water, strong acetic acid, and 10 per cent. caustic soda, allowing the boiling in the water to continue for at least 36 hours, or for a shorter time at a temperature of 120° in sealed tubes, and for about 6 hours in the acetic acid. After the action of the soda the tissue remaining is again boiled with dilute acetic acid, then well washed in water, and afterwards placed 24 hours or so in dilute hydrochloric acid to neutralize the alkali; finally the acid is removed by washing the residue in hot water.

Properties.—The *elasticin* thus obtained appears as a brittle yellowish mass, which recovers its elasticity and fibrous appearance if soaked in dilute acetic acid. If digested for 12 hours or so with strong boiling caustic potash a brownish solution is obtained, which, if neutralized with sulphuric acid, will give a precipitate with tannic acid. It dissolves in strong nitric and sulphuric acids, and the solution, if warmed, yields 30 to 40 per cent. leucin but no tyrosin.

The percentage composition of elastin (C 54·32; H 6·99; N 16·75; ash 0·5—ETZINGER) as well as some of its reactions, such as the red coloration with Millon's reagent, seem to indicate its derivation from, and its close connection with, the albumens.

CHAPTER XXI.

LEUCIN AND TYROSIN.

THESE two bodies, which are important proteid derivatives, will be here described in detail.

LEUCIN or **Amido-caproic Acid** $\left[C_6H_{11}(NH_2)O_2 \text{ or } C_6H_{13}NO_2 = \left\{\begin{matrix} C_5H_{10}NH_2 \\ CO.OH \end{matrix}\right.\right]$, belongs to the fatty bodies and is found in many of the organic tissues, particularly the pancreas, spleen, thymus, salivary glands, and also in the lungs and brain. It is a constant decomposition product of albumen and nitrogenized substances, as horn, etc., and can be obtained from any of these by the action of alkalies or acids, or as the result of trypsin digestion or of decomposition. If cheese, for example, is moistened and allowed to decompose, leucin will be formed, and can be removed from the decomposing mass by the action of water.

Tyrosin frequently accompanies leucin, particularly in urine, but the gelatinous tissues furnish no tyrosin.

Preparation.—1. Digest the following mixture for 6 hours at 45° : fibrin and bullock's pancreas 1 kilo. each, water 6 litres, thymol 4 to 6 grams. Then boil and acidulate with acetic acid, filter, and evaporate the filtrate, when leucin and tyrosin will separate. The deposit is to be collected, and by heating it with water leucin, which dissolves readily, can be separated from the tyrosin, which is not so soluble.

2. Shavings of horn form an easy source. Boil a quantity of these shavings for 3 or 4 hours in twice their weight of dilute sulphuric acid (20 per cent.) in a vessel connected with a condenser; then treat with excess of milk of lime or chalk, and boil again for the same period as previously; now filter, and after the addition of a slight excess of sulphuric acid filter again. The filtrate concentrated by evaporation is set aside to crystallize. Purify the crystals by boiling them with water and lead hydrate, filter, pass sulphuretted hydrogen through the filtrate to separate the lead, filter again, and evaporate the filtrate to dryness. The residue, when dissolved in boiling dilute spirit, and the solution cooled and evaporated down to a small bulk, will give crystals of leucin.

3. Fuse dried albumen with its own weight of caustic potash, and when a well-marked yellow color is attained allow the mass to cool, and then digest it in water; filter after some time, acidify the filtrate slightly with acetic acid, and concentrate to a small bulk: tyrosin is first deposited, and then leucin (BOPP).

Properties.—It generally presents itself in white shining lamellæ, that are fatty to the touch, insoluble in ether and chloroform, easily soluble in alkalies and acids, but more soluble in the same fluids when boiling. Leucin is not very soluble in cold water or spirit. It crystallizes from its aqueous solutions in slightly refracting, more or less brown-tinted spherical masses, that exhibit a fine radial striation often associated with the appearance of concentric rings; these balls are made up of a great series of concentrically grouped, very thin, white, glistening plates or fine needles. When pure, the crystals are generally flat, thin and white; but the rounded lumps are more frequent when the leucin is at all impure.

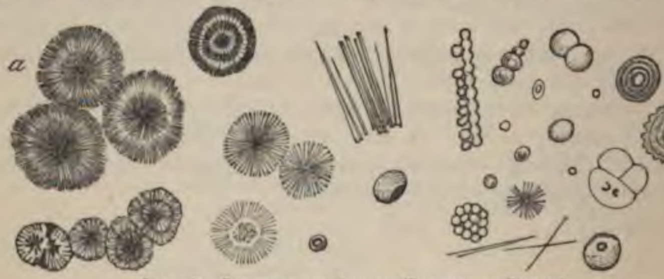


FIG. 15.—CRYSTALS OF LEUCIN (DIFFERENT FORMS).
(Crystals of kreatinin chloride of zinc resemble the leucin crystals depicted at *a*.) The crystals figured towards the right consist of comparatively impure leucin.

It sublimes unchanged at a moderate heat with the odor of amylamine, and condenses in woolly masses consisting of extremely thin rhombic plates, grouped in rosettes.

Leucin forms easily soluble salts with hydrochloric, nitric, and sulphuric acids; it combines also with the salts of lead and silver.

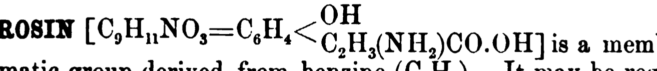
Tests.—1. Place a few crystals on platinum foil, add a drop of nitric acid, and evaporate gently; heat the colorless residue after the addition of a few drops of caustic soda: a yellow or brown mass is obtained, which forms an oily drop (SCHERER).

2. Boil a dilute solution with excess of cupric hydrate, and on cooling bright violet scales are deposited.

To detect in Urine.—Evaporate the urine to dryness; treat the residue with cold absolute alcohol and then extract it with boiling spirits: leucin crystallizes from this on cooling. Examine the deposit under the microscope after 24 hours. The leucin balls may be confounded with those of urate of ammonia, but the latter have a darker contour and are scarcely soluble in alcohol. The deposit may be dissolved in water, basic lead acetate added in excess, filtered, and sulphuretted hydrogen passed through the filtrate to separate excess of lead; the filtrate from this last is evaporated to dryness, and the residue boiled with strong spirit, which dissolves up the leucin but deposits it on cooling. A little of the leucin thus prepared is to be carefully dried and sublimed in a small tube: it is deposited in woolly masses, part of it, however, being decomposed and evolving the smell of amylamine.

To Separate Leucin from Organs in which it is Contained.—Cut up the organ (a pancreas, for example) into little bits, add water, and rub up thoroughly with finely broken glass in a mortar; now express firmly through a cloth, and having acidified the watery extract with acetic acid, boil and filter to separate the precipitated albumen; add basic acetate of lead to the filtrate, filter again, and separate any lead in the filtrate with hydric sulphide. The filtrate from the last is evaporated to a syrup, treated with strong boiling alcohol, and the alcoholic extract evaporated to dryness.

Pathology.—Both leucin and tyrosin may present themselves in urine in acute yellow atrophy of the liver, and in malignant jaundice the crystals of both bodies may be found in the hepatic veins. In the urine it may also be met with in severe cases of typhus and variola (WINIWARTER), and in acute phosphorus poisoning; occasionally also after epileptic fits and brain injuries, and in leucocythæmia. In a few cases both bodies have been seen in the saliva and bile.



TYROSIN $[C_9H_{11}NO_3=C_6H_4<^{OH}_{C_2H_3(NH_2)CO.OH}]$ is a member of the aromatic group derived from benzine (C_6H_6). It may be regarded as an alanin in which hydrogen is replaced by oxyphenol. As a normal constituent of the body it does not probably exist except as a product of pancreatic digestion (RADZIEJEWSKY).

Almost all proteids furnish this body under the action of strong oxidation agents; thus it is obtained by the decomposition of albumen, gelatin, horn, elasticin, and mucin under the action of acids and alkalies, and by the pancreatic digestion of albumens, etc., it has likewise been prepared synthetically (ERLENMEYER).

Preparation.—1. *From Horn Shavings.* Boil 1 kilo. with 2 kilos. strong sulphuric acid and 10 kilos. water for 16 hours; dilute the hot mass with three times its volume of water, and neutralize with thin milk of lime; filter and wash the precipitate with boiling water. Evaporate the filtrate and washings to half their volume, acidify with sulphuric acid, and filter again; add acetate of lead in excess to the filtrate, filter, pass hydric sulphide through the filtrate, and after having boiled for some time throw upon a filter, and evaporate this last filtrate until crystallization begins, assisting the process by the addition of some acetic acid. To purify the crystals dissolve them in water, treat the solution with acetate of lead, separate the lead by a current of sulphuretted hydrogen and subsequent filtration, and evaporate the filtrate; the crystalline residue may be further purified by recrystallization from ammonia.

2. *Preparation by Pancreatic Digestion.*—Take the pancreas of an animal that has been killed some 5 or 6 hours after a large meal, dry it rapidly between some folds of blotting-paper and weigh it; then cut it into pieces and rub up in a mortar with 10 times their weight of raw fibrin; now add about 15 times the weight of the mixture of warm water (45°), and transfer the whole to a hot chamber the temperature of which is steadily maintained a little below 50°, the mixture being stirred from time to time; and after 5 hours or so any albumen present is separated by acidifying with acetic acid, boiling, and filtering through linen. The filtrate is to be quickly reduced to a syrup by evaporation, poured hot into a flask, and alcohol added till an evident precipitate is formed. Filter after some time and evaporate the filtrate to a small bulk. This concentrated filtrate must now be set aside in a cool place for a couple of days, and then the precipitate is to be collected on a filter and washed with cold water. Leucin and tyrosin are both present in the crystalline mass. By washing the deposit well with water at 50° the lucin is separated, and by dissolving the residue in hot water and repeatedly crystallizing this deposit from its solution in ammonia the tyrosin will be obtained in tolerable purity.

Properties.—Tyrosin appears mostly in fine, long, white, silky needles, occurring generally in sheaf-like bundles or rosettes, but appearing frequently as a deposit of yellowish green crystalline globules, which dissolve in hot dilute ammonia, but are deposited on cooling the solution in *brilliant colorless needles, generally grouped in radiated stars.* The crystals somewhat resemble those of hypoxanthin.

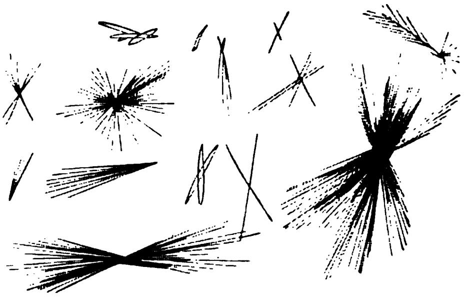


FIG. 16.—TYROSIN CRYSTALS.

Heat decomposes it, so that it does not sublime like leucin. It is insoluble in absolute alcohol and ether, almost insoluble in cold water, and slightly soluble in hot water, but readily soluble in the mineral acids, in warm dilute ammonia, and the other alkalies and alkaline carbonates; soluble, however, with difficulty in acetic acid. It combines with acids and metallic bases, as $C_9H_{11}NO_3.HCl$, $C_9H_{10}NaNO_3$, and $C_9H_{10}AgNO_3$.

Tests.—1. Pour a few drops of strong sulphuric acid over a little tyrosin in a porcelain dish or a watch glass; heat gently for some time over a water bath, and lay aside covered for half an hour; then dilute with water and saturate by rubbing it with a little carbonate of lime or baryta, filter, and evaporate to a few c.c., and filter again from any carbonate of baryta that may separate. Now treat the filtrate with a little *very dilute* neutral ferric chloride solution, and a marked violet color appears (PIRIA).

2. Treat a hot watery solution with a few drops of Millon's reagent, carefully avoiding excess, and boil a few minutes: a rosy or a dark red color appears, and if the solution is concentrated a dark red precipitate may be formed (HOFFMANN).

Or warm the tyrosin solution with the mercuric nitrate obtained by the precipitation of mercuric chloride with silver nitrate.

3. Heat with a drop or two of nitric acid (strong nitric acid and water, equal parts) on platinum foil or porcelain, and evaporate at a gentle heat: a shining yellow residue of brownish yellow crystals of nitrotyrosin nitrate, $C_9H_9(NO_2)NO_3.HNO_3$, is obtained; this becomes reddish yellow and then brownish on the addition of caustic potash, and leaves a brown residue on evaporation (SCHERER).

Many other bodies, such as sarkin, react similarly.

Under Leucin it has already been stated that this body appears in *pathological* conditions in the liver, pus, sputum, etc., and in the urine in acute atrophy of the liver and phosphorus poisoning, etc.

BOOK II.

DIGESTION AND THE SECRETIONS CONCERNED.

CHAPTER I.

FERMENTS; FERMENTATION; AND DECOMPOSITION, OR PUTREFACTION.

BEFORE considering the subject of digestion in detail the opportunity may be here taken of referring to fermentation, which has so much to do with some of the digestive processes. And at the same time, to render the matter more complete, brief reference will be made to an allied process, that of decomposition, in which certain organic ferments play such an active part.

FERMENTS.—The action of these bodies was compared by LIEBIG to that of platinum black in determining the union of a mixture of hydrogen and oxygen. In both fermentation and putrefaction a new arrangement of the elements occurs, generally associated with an assimilation of the components of water, and resulting in the formation of new products. In putrefaction offensive odors are evolved which is not the case with fermentation; and while neither process can be regarded as one simply of oxidation, the *presence of oxygen appears to be necessary to set up the change.*

All fermentation processes *require also the presence of water*, and a proper degree of dilution appears to be more or less essential. A free acid, and that in a very dilute form, seems to be needed in only a few cases, as in gastric digestion, while in most other fermentation processes an acid is in the way, if not positively hurtful. The caustic alkalies also, if above a very minute proportion, hinder fermentation processes completely, and the same may likewise be said of the salts of the heavy metals, as iron, lead, mercury, etc., if present in sufficient quantity, while some fermentations are prevented by the presence of ether, chloroform, etc.

Ferments such as pepsin and trypsin, when dried, may be heated up to 170° without their properties being impaired, but in the moist state a temperature of 100° is sufficient to destroy them (HÜPPE).

PASTEUR distinguishes two kinds of fermentation, one in which the ferment does not require the presence of oxygen (as the butyric) and one in which oxygen is essential in promoting the process.

Ferments may be *divided into the organized and the soluble.* While the living organized ferments, such as yeast, reproduce themselves during their period of activity, the soluble ferments, such as ptyalin, pepsin, etc., do not do so. All fermentation produced by an organized ferment is arrested by hydrogen dioxide and the ferment is killed; but the soluble ferments are not acted on by it (BERT and REGNARD). Borax, on the other hand, destroys the activity of all soluble ferments so decidedly that it serves as a test between the soluble and the organized class (DUMAS and SCHÜTZENBERGER). As a general rule it may be said that all purely *physiological* fermentations in the organism are brought about by the soluble ferments, while *pathological* fermentations, on the other hand, are due to the organized series (EWALD).

In classifying these fermentation processes HOPPE SEYLER'S arrangement will be adopted.

I. Change of Anhydrides into Hydrates.

A. *Ferments that act like Dilute Mineral Acids at a High Temperature.*

1. The conversion of starch into sugar, or glycogen into dextrin and grape sugar—

$$4(C_6H_{10}O_5)+3H_2O=C_6H_{10}O_5+3(C_6H_{12}O_6).$$

glycogen. dextrin. grape sugar.

2. The conversion of cane into grape sugar—

$$C_{12}H_{22}O_{11}H_2O=C_6H_{12}O_6+C_6H_{12}O_6.$$

grape sugar. sugar of fruit.

3. The conversion of different benzol glucosides into sugar and simple benzol derivatives by the action of emulsin—

$$C_{13}H_{18}O_7+H_2O=C_6H_{12}O_6+C_6H_4CH_2(OH)_2.$$

salicin. saligenin.

B. *Ferments that act like Caustic Alkalies at a High Temperature— Fermentative Saponification.*

1. Splitting up of fats into glycerin and fatty acids. The process is favored by the presence of carbonate of lime and of neutral or alkaline solutions. The pancreas contains such a ferment, but it is so readily destroyed that it cannot be separated. A similar ferment also seems to be present in many decomposing substances.

2. Splitting up of amido-compounds by hydration through decomposition ferments; as—

$$CON_2H_4+2H_2O=(NH_4)_2CO_3$$

urea. ammonic carbonate.

$$C_9H_9NO_3+H_2O=C_2H_5NO_2+C_7H_6O_2$$

hippuric acid. glycin. benzoic acid.

$$C_{20}H_{45}NSO_7+H_2O=C_2H_7NSO_3+C_{24}H_{40}O_5.$$

taurocholic acid. taurin. cholic acid.

Possibly the decompositions of albumen effected by trypsin or putrefaction belong to this category.

II. Fermentation Processes with Transferrence of Oxygen from the Hydrogen to the Carbon Atoms.

1. *Lactic Acid Fermentation.*—Various kinds of sugar and dextrin, under the action of special ferments, as *penicillium glaucum* or *bacterium lactis* (LISTER), are converted into lactic acid. A decomposing albuminous substance, especially casein, water, and a temperature between 30° and 35° are required; the presence of chalk or alkaline carbonates favors the process by neutralizing the acid as it is formed, which would otherwise prevent the continuance of the fermentation.

In the first stage lactic acid is produced—

$$C_6H_{12}O_6=2C_3H_6O_3$$

$$C_{12}H_{22}O_{11}+H_2O=4C_3H_6O_3—$$

and in the second stage butyric acid, carbonic anhydride, and hydrogen being evolved—

$$2(C_3H_6O_3)=C_4H_8O_2+2CO_2+2H_2.$$

These processes, particularly the first, probably occur in the intestine.

2. *Alcoholic or Vinous Fermentation.*—In this alcohol and carbonic acid are formed by the conversion of sugar in presence of certain minute living organisms, as *torula cerevisiæ*, the fermentation being a correlative phenomenon of a vital act, beginning and ending with it, an organization, development, and multiplication of the ferment particles occurring simultaneously with the fermentation.

$$\underset{\text{grape sugar.}}{\begin{array}{l} CH_2OH \\ 2(CH.OH) \\ 2(CH.OH) \\ COH \end{array}} + 2H_2O = \begin{array}{l} CO(OH)_2 \text{ carbonic acid.} \\ \left.\begin{array}{l} CH_3CH_2OH \\ CH_3CH_2OH \end{array}\right\} \text{alcohol.} \\ CO(OH)_2 \end{array}$$

In *acetous fermentation* the alcohol is converted into acetic acid under the influence of the *mycoderma aceti*, which acts as a sort of oxygen-carrier.

What is called *mucous fermentation* may be undergone by sugar when in presence of certain nitrogenous substances, hydrogen and carbonic anhydride being evolved, and mannite, lactic acid, etc., being formed.

3. *Decomposition Processes.*—These occur most readily between 25° and 45°, and the part of the ferment appears to be played by such low organisms as the micrococci and bacteria. Heating them with water above 53° seems to act more or less destructively upon their vitality.

$$\underset{\text{calcic acetate.}}{Ca(C_2H_3O_2)_2} + H_2O = CaCO_3 + CO_2 + 2CH_4$$

$$\underset{\text{cellulose.}}{nC_6H_{10}O_5} + nH_2O = 3nCO_2 + 3nCH_4$$

$$\underset{\text{calcic lactate.}}{Ca_2(C_3H_5O_3)_4} = CaCO_3 + 3CO_2 + 4H_2 + \underset{\text{calcic butyrate.}}{Ca(C_4H_7O_2)_2}.$$

Glycerin and carbonate of lime with decomposing fibrin furnish, without access of air, butyric, butyracetic, and succinic acids; probably lactic acid first of all appears, and this splits into carbonic and butyric acids, very little hydrogen being evolved.

Fermentation processes occur in the intestine, and it is very probable that they may also manifest themselves in the interior of living organic cells as well; and although the ferments act possibly by catalysis or contact action, they do not remain entirely unchanged, part of them breaking down and undergoing changes of some kind with which we are unacquainted.

SCHMIEDEBERG describes a soluble ferment, *histozym*, by which many decomposition and synthetic processes occur in the body; thus, according to him, the change of benzoic into hippuric acid in passing through the kidney is due to the influence of this body. It can be extracted by glycerin, from which it is precipitated by alcohol as a white chalk-like mass. The quantity of this body in the blood or organs is very variable, the dog's liver and pig's kidneys being the richest.

BÉCHAMP holds that certain *microzymas*—a name applied to peculiar molecular granulations that appear in various fermentations before any other organized production occurs—exist in the organism, and he regards them as the organized ferments, which act as active chemical and physiological agents, whereby are effected the transformations in the organism both during life and after death. PASTEUR also inclines to accept the existence of these bodies, as he has found that all the natural earths he had occasion to examine contained germs capable of inducing a peculiar fermentative or septic action.

The microzymas, which, according to BÉCHAMP, form an integral part of every living organism, lead to the total destruction of this organism after death; and this having been effected, they remain embedded in the soil or distributed through the air. But while BÉCHAMP regards these granules as living organisms, GAUTIER looks upon them as a purely chemical ferment, without organization and without life.

When proteids and other organized bodies decompose, which they readily do when exposed to damp air, a series of simple products are formed; the name *putrefaction* is generally given to these decomposition fermentations when they occur in animal or vegetable organisms rich in such bodies, and as putrefaction is essentially a process of hydration it follows that the aromatic derivatives and the bases formed during the fermentation pre-exist as nuclei in the albuminoid molecule. In putrefying they lose their coherence, absorb oxygen, and emit fœtid odors, soon also disengaging carbonic acid, nitrogen, hydrogen, ammonia, certain hydrocarbons, and bodies containing sulphur and phosphorus; and when the putrid fermentation is complete, a humid substance rich in fats, in earthy and ammoniacal salts, and in phosphates and nitrates, remains behind. Now, as PASTEUR showed, these changes are not the simple result of spontaneous decomposition; for if the proteids are protected from the entrance into them of the atmospheric germs, they can long be preserved unchanged, but the changes are most probably, as we have already seen, induced by ferment matters or germs existing in the air; and when contact with these bodies is prevented, as by filtration of the air or destruction of the germs by strong heating, the putrefactive processes do not occur. But while a temperature of 60° is sufficient to destroy most of these organisms some of them require a temperature higher than 150° to destroy any undeveloped spores that may be present (DALLENGER, COHN). It seems, indeed, to be fairly proved that bacteria are the active agents in decompositions, and that these bacteria come from without, and are not developed spontaneously in the decomposing fluid or substance (PASTEUR, TYNDALL).

A word or two may be said here as to these bacteria and their congeners. The term *schizomycetes* is applied to the group of small unicellular organisms, including *bacterium*, *vibrio*, *termo*, *spirillum*, *leptothrix*, etc., which multiply by transverse division, either remaining connected or becoming isolated; they exist chiefly on nitrogenous compounds, which, even when insoluble in water, are rendered fluid by the agency of bacteria. When the nitrogenous substance in which the bacteria multiply is completely used up, these bodies pass into a stationary condition and become congregated into gelatinous colonies—the so-called *zoöglea* form—in which they can resume their activity under favorable conditions. These organisms may be divided into several groups, as sphærobacteria (micrococci), microbacteria, desmobacteria, and spirobacteria, in each of which may be distinguished pigment-forming, zymogenous, and pathogenic varieties.

The bacteria are for the most part minute rod-like, oblong or globular protoplasmic masses, varying between $\frac{1}{100000}$ and $\frac{1}{300000}$ of an inch in diameter, enclosed in a structureless substance. Such forms as the *vibriones* appear to possess a wriggling motion, and in some a cilium has been detected.

All fluids containing decomposing organic substances have some of these bodies present, and usually in great numbers. When such fluids evaporate the bacteria germs are carried into the air, and hence become causes of putrefaction in nitrogenous substances exposed to the air, and may serve as propagators of contagious diseases. Indeed, according to the modern doctrine of the production or generation of disease by germs, the contagious diseases, etc., are produced by certain specific organisms or poisons. In septicæmia, for example, an absorption has occurred of certain fluids whose decomposition has been induced by bacteria, and the system is proportionately poisoned. Fluids also that have been subjected to the action of these bacteria, but subsequently freed from them, have been proved to act as septic poisons to the system (BURDON SANDERSON). Accordingly it would seem that the bacteria themselves are not the germs of the disease, but rather possess the power, under suitable conditions, of generating the *contagium*. In splenic fever bacteria have been discovered in the blood and many organs of the body, and according to KOCH the introduction of such germs into healthy animals brings on splenic fever. By inoculating sheep with the prepared blood of cattle that have died of splenic fever, PASTEUR protected them from taking that disease; and similarly by inoculating chickens with the diluted virus of chicken cholera he protected them from its influence. PASTEUR believes that the protection is due to the organisms introduced by inoculation exhausting the substances in the body which afford them nourishment, and that when the animals are attacked by the real disease the disease germs, however introduced, find no food, and accordingly perish. In addition to septicæmia and splenic fever, it has also been pretty fully established that these micro-organisms are the casual agents in producing anthrax, glanders, gonorrhœa, erysipelas, relapsing fever, and tuberculosis.

Antiseptics.—Certain materials have been found that by their presence protect bodies from putrefactive processes; these are antiseptics. *Disinfectants*, on the other hand, are substances that tend to destroy the putrefactive processes already originated, or to render inert their products already formed.

These antiseptics appear to act in different ways, some, as sodium chloride and alcohol, for example, by their attraction for water; others, as sulphurous acid and the bisulphites, by forming comparatively strong combinations with the substances liable to decompose; others, as carbolic and salicylic acids, apparently by destroying the germs that set up the putrefaction; and others again, as oils and fats, etc., by preventing their entrance into the decomposible body by coagulating its exterior, or covering it with a coating impenetrable to the germs.

KOCH finds *carbolic acid* to be almost without action on the spores of *anthrax bacilli*, these retaining their vitality after 5 days' immersion in a 2 per cent. solution, and 15 days in a 1 per cent. solution; but 1 gram pure carbolic acid showed a marked effect in 1,250 grams of a nutritive solution containing these bacilli. Its destructive power is also much greater at a temperature of about 55° than at a lower temperature. Aqueous solutions of the carbolic acid acted antiseptically, but solutions in oil or alcohol did not manifest any antiseptic properties, which is also the case with salicylic acid, thymol, etc., except when they are used with substances containing water.

The disinfecting action of *sulphurous acid* is uncertain. The only effectual disinfectants, indeed, according to KOCH, besides *chlorine*, *bromine*, and *iodine*, are *mercuric chloride*, *osmic acid*, and *potassic permanganate*, this last only acting in 5 per cent. solutions. In his experiments with anthrax spores he likewise found arseniate of sodium very effective, as also boracic and salicylic acids. FRAENZEL further finds that tubercle bacilli are easily destroyed by such bodies as creasote, camphor, and naphthalin.

The actions of thymol, hydrocinnamic and phenylacetic acids, indol, skatol, kresol, and phenol have been examined by WERNICH,, and he finds the thymol superior to all but the phenol.

Substances effective in checking the germination of spores are corrosive sublimate, some essential oils, and amyl alcohol.

But, as the antiseptics used in surgery do not require to be perfect, it is sufficient for the purpose of the surgeon if the propagation of the organisms is arrested for a time long enough to allow the wound to heal. With the spores of splenic fever, for instance, the development is arrested by a 1 per cent. aqueous solution of phenol, or a 5 per cent. solution of zinc chloride; and this suffices for medical purposes, as, although chlorine, etc., would effectually destroy such spores, they would also severely injure the patient to whose wounds they might be applied.

A great difference exists between *antisepsis and disinfection*—a difference, it may be remarked, that is not generally taken sufficiently into account. Thus, in the case of carbolic acid, at times a 2 per cent. solution acts as an antiseptic, but at other times a 5 per cent. solution is needed. To protect a fermentable substance from the action of schizomycetes is very different to destroying them when actually in contact with the fermentable matter, a small amount of the antiseptic being required in the one case as compared with the other. To render the air of a room antiseptic a large amount of phenol is necessary, but a small quantity in the air is sufficient to preserve sound substances from the attacks of bacteria.

It is possible that most of the present methods of disinfection are insufficient to destroy bacteria, and only exert a temporary influence in arresting their development.

Antiseptics have been used to preserve food. Common salt, sugar, spirit, potassic nitrate, and vinegar have been most frequently employed. For the same purpose other methods, as cold, drying, and exclusion of air, have also been adopted with advantage.

CHAPTER II.

DIGESTION.

AFTER a general sketch of this very important process, whose chemistry is an object of such interest to the physiological chemist, the preparation and properties of the different secretions concerned and of their active ferments will be given, and then the secretions themselves discussed in detail.

The process of digestion commences in the mouth, and continues throughout the alimentary canal till the lower part of the large intestine is reached, its object being to convert the food into a condition fit for absorption into the blood. It consists of a great many different processes, that are in part mechanical and in part chemical, being chiefly of the nature of hydrolytic decompositions (HERMANN); and the absorbed products are still further modified after absorption. The bodies upon which the digestive processes are necessary to admit of this absorption are albumens, gelatins, starches, and fats. The inorganic constituents of food, such as water and salts, and the soluble organic constituents undergo no essential chemical change before being absorbed; while bodies insoluble in any of the juices, as cellulose and elastic tissue, are excreted unchanged.

In the mouth the food is ground into a pulp and mixed with the *alkaline saliva*, which latter converts part of the starch present into sugar; the same process is continued, but rendered slower (if not arrested) in the stomach, and is resumed again under the influence of the pancreatic juice.

In the stomach the action of the *acid gastric juice* begins, and it essentially consists in a chemical solution effected under the agency of a ferment, the food being disintegrated and so mixed with the gastric juice as to form a pultaceous mass—the *chyme*. The solvent action of the juice is, however, confined to the nitrogenous substances present, peptones being formed therefrom and probably rapidly absorbed, although a considerable proportion of the albuminous bodies pass away in the chyme in a state of fine subdivision and mechanical suspension into the small intestine, occasionally accompanied also by even large morsels of solid undigested matters, there to undergo subsequent solution. Salts of the carbonates and phosphates that are insoluble in water are also dissolved by the acid of the gastric juice, and, together with other soluble salts or sugars present, are probably in great part absorbed. SCHMIDT considers that the pepsin and the hydrochloric acid form an unstable pepto-hydrochloric acid, constituting about 0·3 per cent. of the juice, and that gastric digestion consists in a combination of this acid with albuminous bodies; it seems more probable, however, that the pepsin acts entirely as a simple ferment, but requiring the presence of a certain amount of free acid to render it active.

The *chyme* is discharged from time to time into the duodenum, and this may occur soon after the commencement of gastric digestion; but probably much does not leave the stomach till two hours or so have elapsed; and the discharge may not be completed till four or five hours after the entry of the food into the stomach.

The chyme is next subjected to the action of the bile, the pancreatic juice, and the intestinal juice, by which it is gradually converted into *chyle*, and absorbed as such—the *undigested albumens* from the stomach being converted into peptones by the pancreatic, and possibly also by the intestinal juice; the *fats* digested by the pancreatic juice with the help of the bile, and the *starches* by the pancreatic and intestinal juices. A partial precipitation of the peptones and of any pepsin present in the chyme leaving the stomach is effected by the bile in the duodenum.

The *pancreatic juice* converts starch into sugar, emulsifies and saponifies fatty matters, and converts albumens into peptones, part of which is still further decomposed into leucin and tyrosin, the amount of peptone thus broken down possibly depending on the excess or deficiency of proteids and on the rapidity or otherwise of the absorption in the intestine. BRÜCKE is of opinion that some of the proteid is absorbed directly into the lacteals, together with some fat, in the form of alkali albumen, without becoming a peptone, and EICHHORST maintains the same.

With regard to the peptones it has generally been believed that being of easy diffusibility they pass through the alimentary mucous membrane into the blood vessels. Peptone has been found in the blood of the portal vein (DROSDOFF), but only in very small quantity. To account for so little being thus found it has been said that very little unchanged peptone reaches the blood through the mucous membrane; or that it undergoes immediate transformation after its passage through, either in the blood itself or in the liver and muscular tissue; but as peptone, when introduced into the circulation, escapes in great part by the urine, it is possible that its actual transformation occurs in the intestinal mucous membrane itself (HOFMEISTER). There seems also to be some relation between the excretion of the urea and the formation of the peptone, which would point to much of the absorbed peptone being at once broken up into its final products. In HOFMEISTER'S experiments the total amount of peptone in the walls of the stomach and intestine was more than double that present in the blood as a whole, and the quantity found in the walls of the small intestine was fourteen times greater than that present in the walls of the stomach. On the other hand, in the cavity of the stomach there was fifteen times as much present as in its mucous membrane, indicating either that the stomach absorbs less of the formed peptone than does the intestine, or that the peptone disappears more quickly from its mucous membrane. This disappearance of the peptone is a vital act, taking place with unequal rapidity according to the stage of digestion. The property of assimilating peptone, however, belongs not only to the stomach, but also to the intestinal mucous membrane, and whether it is accompanied by a reformation of albumen or by a complete disintegration it is as yet difficult to say. That the peptone rapidly disappears after absorption is shown by the fact that none is discoverable in the blood of dogs twenty-four hours after a heavy meal (SCHMIDT MÜLHEIM). The peptone present in the blood ranges from 0·029 to 0·055 per cent., its maximum occurring seven hours after food. It is probably associated in some way with the corpuscles, and not dissolved in the serum.

The *action of the bile* is only subsidiary to that of the pancreatic juice, assisting in the emulsifying and saponifying of oleaginous bodies, serving moreover as a solvent for solid soaps, but having little or no action on starchy or albuminous materials, and making a better emulsifying agent when acting with the pancreatic juice than when acting alone. It aids also in the absorption of the fatty matters by enabling them to pass more readily through the mucous membrane, an action due to the direct contact of that membrane with the bile; further, it checks fermentations and putrefactions in the intestine, and it appears to stimulate the peristaltic contraction of the muscular coats of the intestinal walls, and at the same time possibly stimulates the intestinal glands to secretion. What the exact *function of the intestinal juice* may be is still a matter of doubt; it has been said to possess the power of digesting any of the different classes of foods; but different authorities have arrived at different conclusions. Thus (1) it has been stated to digest fibrin alone (THIRY); (2) to convert starch into sugar, and fibrin into peptones, the action however, being very slow (DOBROSLAWIN); (3) to convert small portions of albumen, casein, and fibrin into peptones, and starch rapidly into sugar (SCHIFF); (4) partially to digest cooked meat and albumen, to emulsify fats, and to convert starch into sugar (COLIN); and (5) to possess no evident solvent power for fat or albumen, but to change starch into sugar and cane sugar into grape sugar (PASCHUTIN).

We may therefore thus sum up the digestive action of the secretions: (1) The *saliva* converts starch into sugar; (2) the *gastric juice*, albumens into acid albuminates and then into peptones; (3) the *pancreatic juice*, starch into dextrin and sugar, albumens into globulin substance and then peptone, and part of the peptone into leucin, tyrosin, and aspartic acid, and fats into glycerin and the fatty acids, partly also saponifying them; (4) the *bile* assists the pancreatic juice in digesting the fats and acids in their absorption; and (5) the *intestinal juice* possibly completes the digestion of the undigested portions of the food, acting on starches and sugars, and possibly also on some of the albumens and fats.

The *reaction* continues acid some time after the chyme leaves the stomach, while in the lower part of the small intestine it is alkaline, or only slightly acid; but the acid reaction is restored or intensified in the cæcum, owing to an acid fermentation that is set up there. The reaction, it must be said, varies considerably with the nature of the food.

The different *soluble products* of the intestinal digestion *are absorbed by the lacteals or portal vessels*, so that when the intestinal contents reach the large intestine their nutritious constituents have in great part been removed.

As to fluids, there is about as much secreted as is absorbed; so that the intestinal contents are little, if at all, denser on entering the large intestine than on leaving the stomach.

The *peptones and sugar* enter the circulation by the portal system, and the *fats* largely by the chyle of the lacteals.

That absorption is the chief work done in the upper part of the large intestine there can be no doubt, but whether a digestive action also occurs there is still *sub judice*. By the removal of the fluids the intestinal contents are gradually converted into the solid fæces, the color also changing from gray, through orange, to a dirty yellowish brown. The digestion, however, cannot be said to be completed until the fluids absorbed in the stomach and intestines have been subjected to the action of the liver and spleen, etc.

Amount of Fluids Discharged into the Alimentary Canal.—A very large amount of fluid is constantly being poured out into the alimentary canal. According to the estimates given below of the juices secreted it would appear that about twenty-six pounds, if not more, of fluid are discharged into the intestine every twenty-four hours; that is, about twice the whole volume of the blood. But it must be remembered that secretion and absorption are going on simultaneously, and accordingly the estimate of a secretion judged by the amount discharged by a fistula is to be regarded as a very imperfect standard of the total amount secreted under normal conditions when the secretion undergoes rapid reabsorption. Possibly this disturbance of the normal conditions may give rise to the great discrepancies in the quantities of the secretions in the twenty-four hours as given by different observers.

Secretion.	Sp. gravity.	Average amount in 24 hours.	Percentage of solids.
		lbs.	Per cent.
Saliva	1·004 to 1·009	1 to 2	0·4 to 0·6
Gastric juice	1·001 " 1·010	10 " 20	0·5 " 1
Pancreatic juice	1·008 " 1·009	$\frac{5}{8}$ " $\frac{3}{4}$	8 " 10
Bile	1·010 " 1·020	2 " 3	9 " 14
Intestinal juice	1·010	$\frac{1}{2}$ " $\frac{3}{4}$	2 " $2\frac{1}{2}$

CHAPTER III.

PREPARATION OF THE JUICES.

1. **Saliva.** (*a*) *Natural Saliva.*—Collect saliva in a beaker after inducing its secretion by inhaling ether vapor into the mouth, or by chewing a piece of india rubber. When a considerable quantity has been thus obtained, add four times its volume of water, stir it well, and let it stand some time, then decant off the supernatant liquid from the sediment.

(*b*) *Artificial Saliva* may readily be prepared by digesting with water the finely mixed fresh salivary glands of any of the herbivora for several hours, and then straining through linen and filtering.

2. **Artificial Gastric Juice.**—(*a*) Open the stomach of a recently killed pig, or the fourth stomach of a calf, wash it rapidly in cold water, spread it out on a board with the mucous surface upwards, and scrape off this surface with a scalpel or sharp spatula. Rub up the soft mass thus obtained with some fine washed sand; then digest the whole with cold water, stirring frequently, and filter. The juice prepared in this way contains very little peptones, which, however, would not be the case if some time is allowed to elapse after the death of the animal before the stomach is used.

(*b*) Rapidly wash a fresh pig's stomach, mince the mucous membrane of its middle third, and digest this some six to eight hours with

200 times its volume of dilute hydrochloric acid (⅕ per cent.) at a temperature of 35°; decant and filter. The digestion may be repeated with fresh acid. Peptones will be present, which may be separated by dialysis.

To prepare the hydrochloric acid of the above strength (⅕ per cent.) add about 6½ c.c. of the ordinary strong commercial acid to a litre of distilled water and shake together. In the experiments the acid may be used of this strength, or diluted with its own volume of water. An acid, however, that serves well for rapid artificial digestion contains one per cent. by volume of concentrated hydrochloric acid (TUSON). The water in which the albumen is immersed may be acidulated with one per cent. of hydrochloric acid of sp. gr. 1·150 (=0·303 per cent. real acid) (DOWDESWELL), or with only half this amount, and contain about 0·15 per cent. of real acid (PETIT), so as to obtain rapid artificial digestion.

(*c*) Divide the washed and detached mucous membrane of a fresh stomach into small fragments, and after drying them well between folds of filter paper cover them with strong glycerin; lay aside for eight days, then strain the glycerin extract and precipitate it with alcohol; collect the precipitate and wash it with spirit. It is then to be added to two litres or so of the acidulated water (0·1 per cent.), or a little of it may be added when required to the dilute acid (after WITTICH).

The glycerin extract may be filtered through linen, and kept as such, a very good digestive fluid being obtained by adding a few drops of it to some of the dilute acid (⅕ per cent.)

3. **Artificial Pancreatic Juice.**—In preparing this juice it is advisable to employ the pancreas of an animal that has been killed *some four or five hours after a full meal has been taken;* for if the pancreas of a fasting animal is employed scarcely any digestive power may be manifested by its glycerin or watery extract.

(*a*) Cut a fresh pancreas (say of a dog killed some hours after a full meal) into pieces, weigh them, and cover the pieces with absolute alcohol for two or three days; express through linen, and dry the gland substance with filter paper; then rub it up with powdered glass or washed sand, adding for each gram of gland substance 1 c.c. dilute acetic acid (one per cent.); stir well for about a quarter of an hour, and then place the whole in a jar, pouring over it ten times its volume of glycerin. After three days decant, and filter through a piece of muslin and then through coarse filter paper.

(*b*) Make an infusion of the minced pancreas in warm water and neutralize the filtrate, if necessary, with sodic carbonate.

(*c*) Mince the pancreas upon a block of filter paper, and cover the fragments with strong glycerin; filter in two or three days.

4. **Artificial Intestinal Juice.**—(*a*) Kill a dog or rabbit, and rapidly remove the small intestine. Attach the lower end to a tap, and clip the other extremity. Fill the intestine with water two or three times, emptying it after each addition, so as to clear it of its contents. As short a time as possible should be lost in doing this. Now slit the

intestine from end to end, and scraping away the mucous membrane, rub it up with some sand, just as in the preparation of artificial gastric juice, and then digest it with four times its volume of water. Filter through muslin and filter paper in succession after it has stood for an hour or so.

(*b*) The *natural juice* is best obtained after the method introduced by Thiry, which consists in starving a sheep or dog for twenty-four hours, then opening its abdominal cavity and drawing out a loop of the small intestine, which is to be cut at each end without disturbing its other connections, the continuity of the intestinal canal being re-established by connecting the open ends of the tube after the removal of the loop. The loop is closed at its lower extremity and left in the abdomen, and from its upper open end, which is fixed in the abdominal wound, the juice secreted is collected.

5. **Bile.**—Fresh ox bile should be used, or some filtered human bile obtained from the *post-mortem* room.

CHAPTER IV.

THE DIGESTIVE FERMENTS.

As we have already seen, ferments may be living and organized, as in the case with torula, etc., or inorganized, as with the enzymes, soluble ferments or zymases that occur in saliva, gastric juice, etc., A body allied to these animal ferments is diastase, a peculiar nitrogenous substance, resembling vegetable albumen, although not albuminous, which is found in germinating seeds, being derived probably from the gluten, and possessing the power of converting starch into dextrin and glucose.

The following compositions have been assigned to some of these bodies, although it is difficult, if not impossible, to obtain them in a state of purity:—

	C.	H.	N.	S.	Ash.	O.	
Emulsion (of almonds)	48·7	7·13	14·16	1·25	—	28·70	Schmidt.
Diastase (from beer of yeast)	49·6	6·5	11·8	—	—	—	Schlossberger.
Pepsin	53·0	6·7	17·8	—	—	22·5	Schmidt.
Pepsin	51·0	7·2	15·4	—	—	—	Chapoteaux.
Ptyalin (glycerin extract)	43·1	7·73	11·86	—	6·1	—	Hüfner.
Trypsin (glycerin extract)	43·6	6·5	13·8	0·88	7·04	—	Hüfner.
Trypsin (without ash)	46·57	7·17	14·95	0·95	—	30·36	Hüfner.

Schmidt's pepsin is not probably pepsin at all, but rather an albumen peptone holding pepsin; thus an albumen peptone has this composition: C=53·5, H=7, N=15·5, O=22·4, S=1·6.

Although these ferments are probably formed at the expense of albuminous bodies, they have neither their composition nor general properties; as compared with albumens they contain less carbon, but more oxygen, while the nitrogen, according to some observers, is much less. The ash of all these bodies is rich in phosphates.

These ferments dissolve in water and glycerin, their solutions dialysing, but they are insoluble in alcohol. A temperature from 80° to 90° renders them inactive. One part of the salivary diastase or ptyalin is said to be sufficient to convert 2,000 parts of starch into sugar; and while some authorities regard the amount of peptones formed by pepsin in an acid solution as indefinite, provided the peptones are removed by dialysis as they are produced and fresh acid added (BRÜCKE), others regard the action as limited (SCHIFF).

I. **To Show the Action of Diastase.**—This body is first prepared by washing beer yeast with a mixture of water and ether, shaking well, and filtering; precipitating the filtrate with alcohol, and collecting and drying the precipitate. A little of this or of a warm water infusion of malt or germinated barley is added to a large quantity of thick gelatinous starch, and the temperature maintained at about 71° for a few minutes, when complete liquefaction of the starch will occur, and dextrin and glucose will replace it.

Ferments exist in many of the tissues and organs, and to all mucous membranes there seems to belong a common ferment, enzym or zymase, capable of imparting its own mobility of molecule to many other organic bodies. Now the ferment in any organs or liquids can be obtained by exposing them thoroughly to the action of absolute alcohol for a week or two, so as to coagulate their albumen, and then exhausting the hardened tissue or precipitate with glycerin, from which the ferment can be afterwards thrown down by alcohol after WITTIG'S process.

II. **Preparation of Ptyalin.**—1. Mince up the fresh salivary glands of a cow and make a watery infusion, and to this (or to saliva itself) add excess of dilute phosphoric acid; then neutralize the filtrate with lime water or milk of lime, and the ferment will be precipitated along with the acid, albumen being thrown down at the same time, but it adheres more closely to the lime than does the ptyalin. Collect the precipitate on a filter, and wash it with a little water, which dissolves out the ptyalin, and this in turn is separated from the water by the addition of five to six times its volume of alcohol. Dry the flocculent precipitate *in vacuo*. By dissolving it up again, reprecipitating with alcohol, and drying it *in vacuo*, as before, it is obtained in a purer form (after COHNHEIM).

The ferment may also be obtained by shaking up the watery infusion with a saturated ethereal solution of cholesterin or collodion.

2. Rapidly mince the perfectly fresh salivary glands of an ox, sheep, or rabbit and cover with absolute alcohol for several days in a flask; then collect in a linen filter, express the spirit thoroughly (or, if necessary, the alcohol may be distilled off at a low temperature), and expose the gland substance to the air to dry. Transfer the dried mass to a mortar, where it is to be rubbed up into a fine powder and then mixed well with glycerin; now pour all into a flask, and cover

with fresh glycerin, shaking occasionally. The glycerin extract is to be strained off and filtered after two or three days. From this the ptyalin is precipitated by alcohol, separated by decantation, and dried in an exhausted receiver over sulphuric acid.

Properties.—Ptyalin forms a white amorphous powder; its solutions in water are precipitated by neutral and basic lead acetate, but not by nitric or tannic acids or by mercuric or platinic chlorides. It has the power of converting starch into sugar, the most favorable temperature being about 35° to 40°, above 60° becoming inactive; diastase, on the other hand, is most active between 60° and 70°.

III. **Preparation of Pepsin.**—1. (After BRÜCKE'S method, which, however, does not furnish *much* pepsin.)

(*a*) Macerate the washed and finely divided mucous membrane of the cardiac end of the fresh stomach of a pig in dilute phosphoric acid (5 per cent.), adding fresh acid until the solution is nearly completed; filter, precipitate the filtrate with excess of clear lime water, collect the gelatinous precipitate of tribasic phosphate of lime and pepsin on a linen filter in which it is to be thoroughly expressed; then digest it with glycerin, which extracts the pepsin.

(*b*) Or the precipitate may be dissolved in dilute hydrochloric acid (about 2 per cent.), precipitated afresh with lime water to separate albumens, and to the filtrate a cold saturated solution of cholesterin in a mixture of ether (1) and alcohol (4) added; shake well together, when the precipitated cholesterin will rise to the surface, carrying the pepsin with it. Collect on a filter, and wash with water, dilute acetic acid and again with distilled water till no precipitate is given with silver nitrate. Then digest the residue with ether so long as the ethereal extract leaves a residue on evaporation. Dry what remains at a low temperature, and a grayish white substance is obtained.

(*c*) The precipitated phosphate of lime and pepsin may be dissolved as in (*b*) in dilute hydrochloric acid (2 per cent.), again precipitated with lime water, expressed as before, and more of the dilute phosphoric acid added, a little at a time and at long intervals; wash the precipitate repeatedly with distilled water and dilute phosphoric acid. The pepsin is now present in a moderately pure condition, and may be separated with glycerin as in (*a*) or (*b*).

2. *Glycerin Extract.*—Cover the dried and finely minced mucous membrane with absolute alcohol, and after 24 hours throw it upon some muslin and express out the spirit; then transfer the mass to a beaker or flask and cover it with glycerin. Filter through muslin after some days, and then through filter paper, and precipitate the pepsin from the filtrate by the addition of an excess of absolute alcohol. Collect the precipitate and dry it as before (after WITTIG).

The glycerin solution contains comparatively few foreign bodies. Glycerin is slow in dissolving up the pepsin, but the addition of a very little acid greatly facilitates the solution; and the mucous membrane in the neighborhood of the pylorus yields up its pepsin more readily if it has been previously treated with sodic chloride solution (GRÜTZNER).

Properties.—Pepsin is a yellowish or grayish white powder, soluble in water and glycerin, but insoluble in alcohol. A watery solution does not diffuse; it gives none of the albumen reactions, nor any precipitate with silver nitrate, but it is precipitated by the neutral and basic acetate of lead. In the dry state it may be heated up to 110° without losing its properties, but this is not the case with its solutions.

Without the addition of some dilute acid like hydrochloric, phosphoric, or lactic it manifests no specific action. It is without action upon keratin, nuclein, starches, or fats. About 37° to 38° is the temperature most favorable to its activity. The presence of 0·1 per cent. sodic chloride aids the catalytic action of the pepsin, but 0·5 to 1 per cent. of this salt interferes materially with the process, while a saturated solution throws down the pepsin from its solutions. An admixture of bile is likewise detrimental, as also an excess of alcohol. While the presence of arsenic does not interfere with the action of pepsin, that of carbolic acid does so materially.

IV. **Preparation of Pancreatic Ferments.**—1. Some of these may be separated in the same way as ptyalin (II., 1 or 2), using the fresh minced pancreas instead of the salivary glands. The ferment thus obtained acts very energetically upon starch between 37° and 40°. It converts glycogen at 12° into sugar. The presence of carbonate of soda is unfavorable to this starch conversion, and a temperature above 70° stops the change, although the dry powder may be heated to 100° without sustaining injury.

2. Kill a dog six hours or so after a full meal, wash out the pancreas through its vessels with iced water, then cut the pancreas up small and rub the pieces in a mortar with clean sand; macerate the product for two hours with 4 or 5 times its volume of water at 25° to 30°.

(*a*) Filter the decanted liquor through linen, and calcined magnesia in excess to the filtrate, filter again into a large flask, and drop slowly into the filtrate one-third its volume of thick collodion: shake vigorously, and having poured the mixture into a wide beaker, leave it to evaporate at a gentle heat, stirring constantly with a glass rod until the ether has escaped. When the precipitate presents a fine granular appearance, separate it by filtration through linen or muslin, and treat it as follows, reserving the filtrate for the separation of the diastatic ferment: wash the precipitate with alcohol, and extract it with a mixture of alcohol and ether: the undissolved residue is then deprived of any alcohol and ether present in it by evaporation, when it is treated with water and the peptone ferment dissolved up, forming a yellow solution, from which the ferment can be precipitated by alcohol.

The ferment thus obtained plays a part more or less like pepsin, acting better, however, in the presence of an alkali than of an acid. It forms a yellowish white amorphous powder insoluble in alcohol, but easily soluble in water or glycerin.

(*b*) The filtrates from the collodion precipitates are rapidly evaporated to one-sixth their combined volume under an exhausted receiver, absolute alcohol added, and the whole laid aside for a couple of days: the precipitate thus formed is first washed with strong spirit and then with a mixture of 2 parts alcohol and 1 part water. Filter again, evaporate *in vacuo*, and dialyse the concentrated liquor: to the contents of the dialyser further concentrated *in vacuo* absolute alcohol is finally added to precipitate the diastatic ferment (after DANILEWSKI).

Hüfner, by macerating in glycerin a pancreas whose fragments had lain several days in alcohol, obtained an amorphous ferment having all the properties of pancreatic juice, and acting on starch, fats, and albumens.

Wittich extracts in a similar way by mincing the pancreas of an ox, leaving it twenty-four hours in alcohol, and then digesting with glycerin. The filtered extract is precipitated with alcohol.

With regard to the properties and characters of these pancreatic ferments and their origin, etc., see under Pancreatic Juice.

V. **Preparation of Liver Ferment.**—There are probably two ferments in the liver, a diastatic or sugar-forming ferment and a butyric acid ferment (Pribram). The diastatic ferment is thus prepared: Cut the fresh liver into pieces, and dry them with blotting-paper; then break them up into a fine pulp, adding a few drops of phenol, and having spread the pulp out in a thin layer on a piece of porous porcelain, dry it at 30°. The dried and pulverized mass is subsequently macerated for three days in glycerin. The glycerin extract is next precipitated with alcohol, and the precipitate redissolved in glycerin.

Sodium chloride and sulphate in 5 per cent. solutions do not affect its action; but the alkalies retard it, while the acids hinder or retard it according to the amount present.

Ferments have also been obtained *from muscle*, one analogous to ptyalin (Piotrowsky) and another apparently identical with pepsin (Brücke); and possibly also a third ferment is present, which causes the *post-mortem* formation of sarcolactic acid.

CHAPTER V.

DIGESTION METHODS AND EXPERIMENTS.

I. Conversion of Starch into Sugar.

A. *By Saliva.*—As saliva converts starch into sugar it is advisable for the student first to perform the tests for starch and sugar on pp. 67, 78, and 79.

1. *Prepare some starch mucilage* by rubbing a little starch into a thin paste with two or three c.c. cold water, and pouring it into 400 c.c. boiling water; then boil for five to ten minutes, and when cool decant the clear liquid.

2. *Conversion of Starch into Sugar by Action of Saliva.*—(*a*) Add a little of the diluted saliva to some starch mucilage contained in a small beaker, and lay it aside for ten minutes or so in a hot chamber about 35° to 40°. It will also serve fairly well to place the beaker some time in water about 40°, or to *gently* warm it in a test tube over a flame, taking care, by bringing the test tube from time to time in contact with the palm of the hand, that the temperature does not rise much above 35°.

(*b*) Now apply the tests for starch and sugar, and it will be seen that sugar has been formed, and that the starch has disappeared in whole or in part.

(*c*) *Influence of Temperature, etc.*—The same process should be repeated as in (*a*), with fresh portions of starch mucilage and saliva, but *with the conditions altered:* thus, if a portion is *boiled*, the action of the salivary ferment is destroyed and no sugar is formed; if the action is allowed to go on at a *low temperature*, it will be greatly retarded; and if at 0° C. it will be entirely arrested for the time being. Note also that with *raw starch*, say that of the potato, the conversion is very slow indeed.

(*d*) *Influence of the Presence of Acids or Alkalies on the Process.*—(j) Add variable amounts of hydrochloric acid to a mixture of starch mucilage and saliva, trying first a $\frac{1}{5}$ per cent. and then a 10 per cent. solution, and it will be found that while the dilute solution apparently retards the process the stronger solution completely stops it.

It therefore follows that the normal acidity of the stomach, which is about that of the $\frac{1}{5}$ per cent. solution, does not entirely prevent the saliva swallowed from continuing to act on the starch present (SCHIFF).

(ij) Note the retarding effect produced by the presence of even a small percentage of caustic soda or potash.

B. *By Pancreatic Juice.*—Add a little glycerin extract of pancreas to some of the starch mucilage, and proceed exactly as in A, 2, and it will be found that the results are the same.

C. *By Intestinal Juice.*—Add a little to some starch mucilage, warm gently, and test as before for sugar.

This juice further *changes cane into grape sugar.* Mix a little of the cane sugar solution with some of the juice, and lay aside for twenty minutes or so in a warm chamber (about 40°). Test before and after with Fehling's solution: the cane sugar has little reducing power, but after the action of the juice it reduces the copper rapidly, with the formation of the red or yellowish precipitate of cuprous oxide.

The result, then, of the action of these juices on starch is to convert it into grape sugar—*from the state of a colloid, in short, into that of a crystalloid.* Note this by placing starch mucilage in one dialyser and solution of sugar in a second, and examine the fluids in which the dialysers float after twenty-four hours, when traces of sugar will be detected, but none of starch.

It may here be mentioned that according to some recent researches (WORTMANN) bacteria possess the power, under certain conditions, of acting on starch in a manner analogous to diastase, a ferment appearing to be secreted by them which, like diastase, is soluble in water and precipitable by alcohol, capable also of acting on the starch in the absence of oxygen, slightly acid solutions expediting the process.

II. Conversion of Albumens into Peptones.

A. *By Gastric Juice.*

1. *Formation of Peptones.*—Provide fragments of the following: washed fibrin that has been boiled, boiled or roast meat, white of boiled egg; also some fresh milk. Place them separately in small flasks and cover them with artificial gastric juice; then loosely cork them and lay them aside in a warm chamber at a *uniform* temperature of 38° to 40°

for several hours, and examine them from time to time, shaking them also frequently. A slight increase of the temperature up to 50° promotes the digestion, but the process is materially retarded by the temperature being lowered even a few degrees below 38° or raised above 50°.

(*a*) On examination it will be observed that the solids have swollen up, and have lost somewhat of their opacity, while the milk has undergone coagulation from the precipitation of the casein. Later the solids fall asunder and are digested completely.

(*b*) A few c.c. of the clear fluid are to be removed with a pipette from each of the small flasks every fifteen to twenty minutes for the first hour, and again after two hours from their first having been placed in the hot chamber. This fluid is to be *boiled*, when it will be seen that *coagulation occurs readily* with the specimens removed at first, but that later the amount of coagulum becomes less and less, until *at last no permanent cloudiness or indication of a precipitate occurs*, although before this is found many hours must have elapsed. At this point remove a fresh quantity from the flask, and neutralize it carefully, when a precipitation takes place. That is, the albumen has been changed into a body *which does not coagulate on boiling*, *and which is thrown down by neutralization*. This is *acid albumen*, or, as it has also been termed, *parapeptone*, *syntonin*, *or albumose*.

(*c*) Examine specimens at a still later period, say after the lapse of four or even ten hours. (But if the peptones are required earlier, or in larger quantity, digest a considerable amount of the proteid with the juice, and after a couple of hours decant and filter through coarse filter paper; neutralize the filtrate accurately, and if any precipitate of acid albumen occurs, filter it off, and the peptones will be obtained in this second filtrate.)

(1) Boil—no precipitate.

(2) Neutralize—no precipitate.

Acid albumen is therefore no longer present, but a new body, *peptone*. Apply to the solution the different tests given under *Albumen*, noting that—

(1) It gives the protein reactions—Millon's, the xanthoproteic, and a purple red coloration with excess of Fehling's solution.

(2) It dialyses.

(3) It is precipitated by alcohol, and by strong solutions of mercurous and mercuric nitrate and mercuric chloride, plumbic ammonio-subacetate, and tannic acid.

(4) It is not precipitated by acids or alkalies, acetic acid and potassic ferrocyanide, nor by cupric sulphate or earthy salts.

2. *Influence of Excess of Acid*, *Temperature*, *etc.*—Place fragments of the boiled fibrin in three additional flasks, and add to these respectively (1) 10 c.c. dilute hydrochloric acid ($\frac{1}{5}$ per cent.), (2) 10 c.c. artificial gastric juice that has been *boiled*, and (3) 10 c.c. of the same juice that has been exactly *neutralized*. These flasks, when labelled, are to be placed in the hot chamber (at 40°) and occasionally examined. (4) A small flask containing fibrin and artificial gastric juice is to be placed in an *ice chamber;* and (5) three other flasks with the same contents as in (4), but with the fragment of fibrin in the first *firmly wrapped round with silk thread*, and with the addition of some *strong*

solution of sodic chloride to the second, and some drops of *strong hydrochloric acid* to the third, are also to be placed in the hot chamber (40°).

Note: with (1) that no peptone has been formed, acid albumen only being present, which is shown by its precipitation when the fluid is neutralized. Acid alone is therefore incapable, or nearly so (WITTICH), of forming peptone. With (2) the same result as with (1), the action of the pepsin having been destroyed by the boiling, and the acid alone acting. With (3) the fibrin remains unaltered, the pepsin not acting on the fibrin in the absence of free acid; but that the action is only suspended can be shown by adding more dilute hydrochloric acid. With (4) it will be seen that the low temperature stops the action; while in (5) the digestive action is greatly retarded by the fibrin being prevented from swelling up by the mechanical pressure and by the presence of excess of common salt and of acid.

3. *To show the continuous ferment action of the pepsin,* place some pieces of fibrin in a small dialyser, and having added a sufficiency of artificial gastric juice, suspend it in warm water inside a hot chamber (40°). If fresh acid ($\frac{1}{5}$ per cent. hydrochloric acid, or better dilute phosphoric acid) is poured in occasionally, additional pieces of fibrin may continue to be added without retarding the process, conversion into peptones continuing, which would not be the case if the peptones were allowed to accumulate, but as they dialyse out the action of the juice is not thereby hindered.

For the gastric juice to act advantageously we thus see that it *must contain pepsin,* and that it is necessary for the *temperature to be kept about* 40° C., for a *normal acidity to be maintained,* and for the *peptones formed not to be allowed to accumulate.*

B. *By Pancreatic Juice.*

1. Proceed as in A, using glycerin extract of pancreas diluted with sodic carbonate solution (1 per cent.) instead of the artificial gastric juice, and fragments of boiled fibrin in preference to any of the other proteids.

Peptones will be formed, as with the gastric juice, and it will be found that a temperature about 35°, a moderate degree of alkalinity instead of acidity, and a certain lapse of time are necessary for the conversion. The physical change in the proteids differs slightly from that effected by the artificial gastric juice, as is well seen in the case of the fibrin, where this body appears to be eaten away rather then rendered transparent and dissolved, as with the gastric juice.

2. *Some of the peptone formed is afterwards decomposed into leucin and tyrosin, etc.* Let the digestion go on for a day or two, then acidulate with acetic acid and boil, and if any precipitate occurs filter; evaporate the filtrate at about 65°, and when considerably reduced in volume add to it, while yet hot, alcohol to precipitate the peptones; filter after twenty-four hours, and having evaporated the filtrate to a small bulk, let it cool, *when tyrosin crystallizes out.* The mother liquor, when decanted and evaporated still further, yields *crystals of leucin.* Purify the tyrosin by washing it on a filter successively with ice-cold water, spirit, absolute alcohol, and ether; and after allowing the crystals

of leucin to drain completely on a filter, proceed exactly with their purification as with the tyrosin crystals.

(*a*) *Test the Leucin.*—Note the appearance of the leucin, if pure, in the form of white and glistening, fatty-looking leaflets, and under the microscope often appearing in the form of little glistening balls, occasionally radially striated. Add some crystals to a little cupric hydrate in a test tube, and an intense blue fluid will be obtained on boiling. Or, if the dry crystals are heated in a subliming tube, the leucin will sublime in woolly masses, part decomposing with the odor of methylamine.

(*b*) *Test the Tyrosin.*—It occurs in bunches of felted, silky-looking white needles, though occasionally in hard white balls. Dissolve a few crystals in hot water and boil two or three minutes with a few drops of Millon's reagent, and a rosy red to a dark red color is obtained (HOFFMANN). Or dissolve some crystals in strong sulphuric acid, and heat over a water bath for half an hour; dilute it well with water and saturate with carbonate of baryta, filter, evaporate nearly to dryness, and filter again if necessary; now treat the residue or the filtrate with very dilute ferric chloride solution, when a *violet coloration* is obtained (PIRIA).

(*c*) The ultimate mother liquor is then to be tested for *napthilamine* by diluting a few drops of it with water, and then slowly adding *chlorine water*, when a *rose-red color* appears.

(*d*) Boil a little more of the same diluted mother liquor in a test tube, then add a few drops of *dilute sulphuric* acid and of a *dilute nitrite solution*, and a *red color* shows itself, indicating the presence of *indol.*

Instead of the nitrite a solution may be employed of nitrous acid, readily obtained by filling a small flask with the red fumes of nitrous acid by boiling a little nitric acid with copper foil, then suddenly inverting the flask, and having thus discharged the foil and nitric acid, adding a little cold water and shaking for a few minutes.

III. Digestion of Fats.

A. *By Pancreatic Juice.*—Use a *fresh* watery infusion, as a simple watery infusion, if kept, tends to become acid.

1. *It emulsifies.* Rub a little olive oil or melted lard (of a temperature below 40°) with rather more than twice its volume of the simple watery alkaline infusion of pancreas in a small mortar that has been taken warm out of hot water. A creamy emulsion is formed, which remains as such for several hours.

2. *It also saponifies*, decomposing the fat and liberating the fatty acid and glycerin. Add a little of the watery infusion, that has been carefully neutralized, to a few drops of olive oil in a test tube. Shake well and expose to a gentle heat for a short time. Then, by means of a pipette, transfer a drop from the bottom of the test tube to a piece of blue litmus paper, and a red spot will be left when the drop is thrown off.

B. *By Bile.*—1. Rub some olive oil with an equal amount of fresh ox bile in a mortar, and then pour the mixture into a small flask, where it is to be well shaken for some minutes. *An emulsion is formed*, which remains permanent for a short time.

2. *To show that fatty bodies more readily penetrate membranes moistened with bile than with water*, take two small filters, and after brushing one with water and the other with fresh bile or a watery solution of it, pour an equal quantity of oil into each filter, and leave aside for a few hours, taking care to keep the filters sufficiently moistened on their outer or lower surface with water and bile respectively. It will then be seen that some of the oil has passed through the filter moistened with bile, but none through that wetted with water.

CHAPTER VI.

CHEMISTRY OF THE DIGESTIVE SECRETIONS.

The Saliva.—This is the first secretion to whose action the food is exposed. It is the product of the combined secretion of the parotid, submaxillary, and sublingual glands. In the mouth these secretions are mixed together as well as with the mucus secreted in that cavity itself. The mixed saliva forms a clear or glairy, frothy, and generally turbid fluid without taste or smell, having a sp. gr. of 1002 to 1006, an alkaline reaction, and almost 0·5 per cent. of solids, of which 0·2 consists of salts, and the rest of ptyalin, globulin, and serum albumen. It deposits a sediment in which are epithelial cells from the mouth and salivary corpuscles—little bodies resembling the pale corpuscles of the blood and probably derived therefrom. The alkaline reaction seems to depend on the presence of bicarbonates and phosphates of the alkalies, though the combination of the ptyalin with soda may assist. Saliva from different individuals may show a constant difference in alkalinity, although it varies only within narrow limits; and while showing within certain limits in the same individual a constant degree of alkalinity, there is a decided and constant difference in different individuals, but no constant corresponding difference in diastatic action (CHITTENDEN).

Chemical Composition.—The important bodies present in saliva are the diastatic ferment, ptyalin, mucin, and the chlorides of sodium and potassium; in addition are found traces of albumen, fat, potassic sulphocyanide, sulphates and phosphates of the alkalies and alkaline earths, and sometimes, even in normal saliva, urea and ammonic nitrite.

Mixed Saliva—Human (JACUBOWITSCH).

Water	99·51
Solids	0·48
Soluble organic bodies (ptyalin, etc.)	0·13
Epithelium	0·16
Inorganic salts	0·182
Potassic sulphocyanide	0·006
Potassic and sodic chlorides	0·084

***Mixed Saliva*—Human (Hammerbacher).**

Water	92·42
Solids	0·58
Epithelium and mucin	0·22
Ptyalin and albumen	0·14
Inorganic salts	0·22
Potassic sulphocyanide	0·004

In 100 *Parts Solids.*

Epithelium and mucin	37·98
Ptyalin and albumen	23·97
Inorganic salts	38·03

In 100 *Parts Ash.*

Potash	45·71
Soda	9·59
Lime	5·01
Magnesia	0·16
Phosphoric anhydride	18·85
Sulphuric "	6·38
Chlorine	18·35

1·8 per cent. of the sulphuric acid existed as such, the rest being derived from the organic matter.

Enderlin gives in the 100 parts of ash 92·37 as soluble and 5·51 as insoluble, of which sodic chloride = 61·93, sodic phosphate = 28·12, phosphate and carbonate of lime = 5·51, and sodic carbonate = 2·31.

	Parotid Saliva (Human). (Hoppe Seyler.)	*Submaxillary Saliva* (Dog). (Herter.)
Water	99·32	99·44
Solids	0·68	0·59
Mucin and epithelium	0·34	0·066
Soluble organic bodies		0·17
Potassic sulphocyanide	0·03	—
Inorganic salts	0·34	0·43

Saliva of Horse (Ellenberger and Hofmeister).

	Parotid.	Submaxillary.
Sp. gr.	1006–1007·5	1003
Water	99·16	99·25
Solids	0·84	0·75
Salts	0·59	0·25
Organic matter	0·24	0·49
Acid albuminate	0·008	0·058
Albumen	0·174	—
Fat	0·001	—
Mucin	—	0·358

In 100 *Parts Ash.*

Soluble	93·14
Insoluble	6·86
Sodic chloride	40·05
Potassic "	24·35
Phosphate and carbonate of lime	6·80
Sodic carbonate	23·36

Some authorities give the mucin in submaxillary saliva as about 0·2 per cent., the ptyalin as about 0·11 per cent., and the salts 0·2 per cent., of which the chlorides form 0·07 per cent. and the phosphates 0·08 per cent.

Gases of the Submaxillary Saliva (**PFLÜGER**).

	Per cent.
Oxygen	0·4 to 0·6
Free carbonic anhydride	19·3 " 22·5
Combined "	29·9 " 42·2
Nitrogen	0·7 " 0·8

The secretion is therefore much richer than venous blood in carbonic acid and poorer in nitrogen.

The *parotid secretion* is very clear and watery, and not at all viscid. It contains little or no mucus or formed elements. The reaction of the first secreted saliva is less alkaline than that secreted later, although, according to **ASTASCHEWSKY**, it has a faintly acid reaction that gives place to an alkaline reaction when the mucous membrane of the mouth is slightly irritated. On standing the secretion becomes turbid, owing to the escape of carbonic acid and the consequent precipitation of calcic carbonate. When the saliva is boiled this salt is likewise deposited, and a slight coagulum of albumen is formed. Of the ferment ptyalin about ½ per cent. has been obtained in the human parotid saliva, but only about ⅐ per cent. in that of the horse, while in rabbits and guinea pigs it is more abundant than in man; parotid saliva accordingly is comparatively rich in ptyalin and poor in mucin. It also varies in amount during the day, less being secreted immediately after a meal. As constituents more or less peculiar to it the parotid saliva contains paraglobulin, caproic acid, urea, and traces of sulphates.

The *sublingual saliva* is rich in salivary corpuscles and mucus, and is strongly alkaline, very viscid and thready, and appears to be the richest of the salivas in solids and ptyalin. **HEIDENHAIN** found 2·75 per cent. of solids in the dog. Traces of cholesterin and fat have been met in it.

The character of the *submaxillary saliva* is dependent on the exciting stimulus to its secretion—it is more alkaline than the parotid secretion, and more viscid from the presence of mucus; it is also rich in corpuscles, poor in ptyalin, and has an average specific gravity of 1002 to 1003.

(*a*) *Stimulation of the chorda tympani* or of the lingual, as when acids are applied to the surface of the tongue, causes a normal rich alkaline secretion (*chordal saliva*), but apparently containing no ptyalin; a much quicker stream of arterial blood also traverses the gland; but with long-continued stimulation the percentage of organic solids somewhat diminishes, although at first the mucin is specially increased; strong stimulation also particularly augmenting the organic solids. The secreted saliva is moreover 1° warmer than the arterial blood entering the gland (**LUDWIG**). **HEIDENHAIN** gives the solids as 3 per cent., of which 2·5 are organic and 0·5 inorganic; but by other authorities they are given as 1·2 to 1·4 per cent.

(*β*) *Stimulation of the sympathetic*, or the application of pepper or alkalies to the tongue, causes an outpouring of a strongly alkaline secretion (*sympathetic saliva*) of high specific gravity (1007 to 1018), but it is viscid and turbid, flows slowly, and is very rich in mucus and irregularly formed cell elements. The small arteries are contracted and the current of blood is rendered slower, the venous blood being very dark and poor in oxygen. In this secretion 2·7 per cent. solids may be present (**ECKHARD**), or as much as 5·8 per cent. (**HEIDENHAIN**).

(γ) The secretion may also follow *paralysis of the nerves supplying the gland*, either from *section or curara poisoning* (*paralytic saliva*, Bernard). It is very watery and contains little solids or mucus.

Quantity and Stimuli.—The amount secreted in the twenty-four hours cannot be constant, for estimates varying between 13 oz. and 3·3 lbs. have been given. Its secretion may be excited by the sight or even the thought of food; also by the movements of mastication, the vapors of ether or acetic acid, or by electric excitation. Jacobson's nerve when stimulated causes a watery secretion in which the ptyalin, albumen, and salts are diminished; and when stimulation of the sympathetic occurs simultaneously a copious secretion is obtained containing the organic constituents in abundance together with a slight increase of the salts. In a previous paragraph the stimuli that excite secretion in the submaxillary gland have been referred to in detail. Atropin paralyzes, while pilocarpin and eserin stimulate the activity of the gland.

Functions.—It moistens the food, and by keeping the mucous surface of the mouth wet it assists in mastication and deglutition. Fats are very feebly emulsified by saliva, and soluble substances, such as sugar, are dissolved, thus enabling them to be tasted; but its great function is the conversion of some of the starch of the food into sugar;

$$\underset{\text{starch.}}{3(C_6H_{10}O_5)}+3H_2O=\underset{\text{grape sugar.}}{C_6H_{12}O_6}+\underset{\text{dextrin.}}{2(C_6H_{10}O_5)}+2H_2O=3(C_6H_{12}O_6).$$

According to Mering, however, when starch is acted on by saliva it yields dextrin and maltose ($C_{12}H_{22}O_{11}$) at first, but by a prolonged action some grape sugar is produced as the result of decomposition of the maltose. Two different dextrins also are produced, of which one is attacked by ferments and the other not.

The rapidity of the conversion of the starch depends not only on the quality of the saliva, the parotid acting more slowly than the submaxillary, owing to the smaller proportion of pepsin present in it; but also it is affected by the quality and aggregation of the starch. The diastatic ferment on which the property depends is destroyed, as we have already seen, by a high temperature, by the rapid action of strong acids and alkalies, or by the prolonged action of weak acids or alkalies. Chittenden and Griswold find that the presence of acid, as hydrochloric, to the amount of 0·005 per cent. decidedly increases the diastatic action, while an increase beyond this diminishes it, the action stopping with solutions of acid from 0·1 to 0·4 per cent.; the diastatic action of the saliva would therefore appear soon to cease in the stomach, but the peptones in that organ exercise a decided influence on salivary digestion, stimulating the ferment to increased action, particularly in presence of acid, which by itself may completely prevent the conversion of starch into sugar.

Peptone-forming ferments have been isolated from the saliva of some animals by Hüfner and Munk, which digest fibrin in presence of 0·02 per cent. hydrochloric acid. Hüfner's ferment acts in an acid as well as in an alkaline medium, but Munk's only in an acid medium.

In addition to its action on starch the saliva also serves to carry away potash salts and excess of water which are absorbed lower down, thus helping to maintain a constant round in the circulation.

Reactions.—1. *When saliva is boiled* it becomes turbid from the the precipitation of albumen; and a similar precipitate can be obtained by the action of alcohol, acetate of lead, mercuric chloride, and tannin.

2. *Ferric chloride* gives with it a blood red color, owing to the presence of potassic sulphocyanide. This red color is removed by mercuric or auric chloride, but not by hydrochloric acid; the presence of alkaline solutions or of energetic oxidizing or reducing agents interferes with its delicacy. The red color resembles that given by *meconic acid*, but the color of the meconate thus formed is not bleached by mercuric chloride. *Acetic and formic acids* also give a red tint, but this is removed by hydrochloric acid. To obtain this reaction satisfactorily it may often be necessary to distil the saliva with phosphoric acid, and test the first of the distillate. The test may also be thus applied; Immerse strips of paper in an amber-colored solution of ferric chloride to which a few drops of hydrochloric acid have been added, and then let them dry. A drop of saliva will give a red spot if applied to the paper thus prepared.

3. Immerse a piece of Swedish filter paper in freshly prepared tincture of guaiacum, and after it has dried pass it through a dilute colorless (about $\frac{1}{20}$ per cent.) solution of cupric sulphate. When a bit of this prepared paper is immersed in saliva it becomes blue at once (BÖTTGER'S test).

4. It gives a yellow or blue coloration on the addition of iodic acid, owing to the liberation of iodine (SOLERA). And the presence of nitrous acid may be shown by the yellow coloration given with diamidobenzol sulphate.

Determination of the Sulphocyanide or Thiocyanate (KCNS).—Dissolve perfectly dry potassic sulphocyanide 0·05 gram in water (say 100 c.c.), and add to it ferric chloride till no more intensity of color is produced; then measure the volume of liquid. This is the test solution *a*.

Now take a definite volume of the saliva, and place it in a small graduated cylindrical glass vessel; add to it a drop or two of hydrochloric acid and ferric chloride with brisk stirring until its maximum of intensity of color is obtained; call this *b*.

Having carefully noted the intensity of tint of *b*, place three or four similar cylinders to that holding the saliva beside it on a piece of white paper in a good light: then add to one of these by means of a graduated pipette a few c.c. of the ferric sulphocyanide solution (*a*); make it up to the same volume as the saliva (*b*) with distilled water. After stirring well note the intensity of color by looking vertically downwards through the column of liquid, and compare it with that of the saliva. If not so deep a red tint, a fresh experiment must be made in the same way, but using more of the sulphocyanide test solution. We thus proceed till an equal intensity of color is obtained in the two columns of liquid. From the amount of the test solution *a* required we can easily calculate the percentage of sulphocyanide in the saliva.

Pathology.—In catarrh of the mouth and intestinal tract the saliva is *acid*, also occasionally acid in carcinoma of the liver and typhus fever, in muguet, and frequently in dyspepsia, though in this last it may be due to admixture with acid mucus. In diabetes the saliva may be acid and contain lactic acid, but this is exceptional; it may have a *fœtid odor* in gingivitus, scurvy, and mercurial salivation; in liver diseases *bile pigments* may show themselves (WRIGHT), though this is denied by HOPPE SEYLER; in Bright's disease *urea* is abundant, and in hysteria *leucin* has been found. The amount may be much diminished in fevers, and in chlorosis it is very poor in organic and inorganic solids. In the period of dentition of children *the amount is abnormally increased;* the same may be sometimes observed in hysteria, and especially after the prolongod use of mercury. In mercurial salivation the secretion is alkaline, rich in solids, especially in mucus, and in fats, salts, and albumen; it is often less transparent, and seldom contains any sulphocyanide; but later it becomes thinner and clearer, and contains sulphocyanide and mercury. After the *use of iodides and bromides* these bodies rapidly appear in the saliva; but neither salts of mercury nor iron are thus excreted, although the former are stated to appear by some observers. That the saliva may become poisonous, or at least much altered in its properties, when secreted under the influence of passion is very probable.

Salivary calculi are occasionally met with, of an elongated form, a dirty white color, and formed of concentric layers. They vary in size, appearance, and composition, but their components are generally—

	Per cent.
Calcic phosphate	30 to 80
" carbonate	11 " 15
Organic matter	5 " 25

The *tartar of the teeth* is of a grayish, yellowish, or brownish color; tufts of *leptothrix buccalis* are generally present; and it consists chiefly of phosphate of lime with a little carbonate of lime and phosphate of iron:

	Per cent.
Calcic phosphate	55 to 64
" carbonate	7 " 8
Ferric phosphate	1 " 3
Residue consisting of organic matter, salts of the alkalies, and silica, etc.	24 " 28

CHAPTER VII.

GASTRIC JUICE.

THE gastric juice is a thin, transparent, faintly yellowish fluid, having an intensely acid reaction, a specific gravity varying between 1001 and 1010, and containing from ½ to 1 per cent. solids, of which two-thirds or less is organic and one-third inorganic.

In addition to the acid gastric juice secreted by the stomach an alkaline juice, or *succus pyloricus* (KLEMENSIEWICZ), is furnished by the pyloric end; while the latter is continuous in its secretion the former is intermittent. The normal juice of the stomach consists of a mixture of these two. The *succus pyloricus* is described as being alkaline, having a specific gravity of 1009 to 1010, and 1·6 to 2 per cent. of solids, and is said to convert starch into sugar, and to digest albumen after the addition of hydrochloric acid, also dissolving gelatin, but having no action on fat. This pyloric juice gives the mucin reactions, as well as a milky flocculent precipitate with nitric acid. In a state of rest the slimy secretion formed by the stomach is alkaline.

Quantity.—The amount is very variable, and very widely differing estimates have been given as to the quantity secreted in the twenty-four hours. BIDDER and SCHMIDT gave it as 14 lbs., C. SCHMIDT and GRÜNEWALD as 24·6 per cent. of the body weight (over 36 lbs.) in the twenty-four hours, or about 18 oz. per hour. It may be stated to vary between 16 to 31 lbs., or an average of 20 pints.

Chemical Composition.—The important constituents are free acid and pepsin; this acid is hydrochloric, and it is the only acid the fresh juice contains, but on standing traces of lactic, acetic, or butyric may show themselves (RICHET). The free hydrochloric acid forms 0·24 to 0·42 per cent. (SCHMIDT); but the mean acidity, according to RICHET, is 0·17 per cent., though it is occasionally as high as 0·32 per cent. and as low as 0·05 per cent. The juice is more acid during digestion, and the amount increases with the process; but the acidity is not so variable as the proportion of pepsin; SCHMIDT gives the latter as 0·3 per cent.; but SCHMIDT'S pepsin, as we have seen, was impure. In the dog the free acid is nearly six times what it is in man, although SZABE is of opinion that the free acid of human gastric juice is much more than is generally supposed (0·3 per cent.)

Analysis of Gastric Juice (Human) mixed with some Saliva.

(After C. SCHMIDT, etc.)

Water	99·44
Solids	0·56
Organic substances (pepsin and peptones)	0·32
Free hydrochloric acid	0·25
Sodic chloride	0·14
Potassic "	0·05
Calcic "	0·006
Phosphates of lime, magnesia, and iron	0·015

When gastric juice is added to a mixture of starch and potassic iodide and iodate, the *free* hydrochloric acid causes a blue color to appear, although the juice does not generally effervesce with bicarbonates. Boiling causes no precipitation of the juice, but a precipitate is given with acetate of lead, and silver nitrate, and alcohol in excess.

In gastric juice we generally meet with some mucin as well as peptones; also traces of fats, while phosphates and sulphates of the alkalies are almost completely absent. Great differences exist in health in the gastric juice even of the same animal, and in dogs, sheep, and horses the solids are more abundant than in man.

According to BÉCHAMP the active organic matter of the gastric juice in the glands of the stomach is formed of isolated microzymas (see page 136), and of microzymas still united as granular nuclei of the glandular cells. In presence of hydrochloric acid this matter, which is a special modification of albuminoid substance, is capable of dissolving fibrin, casein, etc. Simultaneously with the destruction of the cells an organization occurs, and new cells replace those that disappear; and as the production is greater than the consumption the gland does not dissolve.

HAMMARSTEN also describes two additional ferments as present in the stomach, which are concerned in the precipitation of casein from milk and in the conversion of milk sugar into lactic acid. The absence of these ferments in certain pathological conditions of the stomach would explain certain anomalies occasionally observed in the digestion of milk.

Digestive Action.—1. It acts especially on *albuminous bodies*, converting them into peptones, soluble albumens being first coagulated. The amount of the albumens rendered dialysable and assimilable in the stomach varies somewhat with the character of the juice and the duration of their sojourn in the stomach; but gastric digestion is always incomplete, and is only terminated in the intestine. Between albumen and the peptone formed there are certain intermediate products to which different names have been given, although probably they are identical or nearly so, such as albumose, acid albumen, syntonin, parapeptone, etc. Considerable difference of opinion also exists as to the ultimate transformation of the albumen, some regarding it as becoming completely converted into peptone (BRÜCKE), and others considering this transformation to be incomplete, a variable amount of unchanged parapeptone making its appearance at the same time (MEISSNER). The quantity of peptones present in the stomach appears to be practically the same at all times during the digestion, indicating that after the formation of a definite quantity of the digestive products the removal of these bodies keeps pace with their digestion (SCHMIDT MÜLHEIM).

2. *Chondrin* is acted on slowly, cartilages, however, furnishing some sugar as a part of their digestion. In some animals, as dogs, *bones* are capable of partial or complete gastric digestion. *Gelatinous bodies* quickly swell up and dissolve, and in this change ETZINGER thinks that the pepsin alone combines. He found even elastic tissue to be more or less digestible.

3. *Fats are chemically unaltered*, except in so far that the connective tissues or proteid framework in which the fat cells are embedded is loosened and more or less dissolved, and partly also the walls of the cells themselves, so as to set free some of the fat; this is melted, and tends to run into drops, and to be imperfectly emulsionized. If fats are present in large amount they interfere with digestion.

4. The conversion of starch into sugar by the action of the swallowed saliva still goes on (SCHIFF), but possibly more slowly than in the mouth; some maintain, however, that the conversion stops in the stomach. ZAWILSKI states that erythrodextrin as well as achroodextrin are converted into sugar by the action of pepsin alone without acids, even when the entry of saliva is prevented.

5. Certain salts are rendered soluble, carbonates passing into chlorides, phosphates to acid phosphates, etc.

6. The gastric juice prevents certain fermentations and decompositions occurring in the stomach, this being probably due to the presence of free acid.

7. No action appears to occur on horny tissue, mucin, nuclein, amyloid substance, wax, cellulose, saccharine and gummy bodies, except in effecting a simple solution of some of them.

8. The product of gastric digestion is named *chyme;* it is from time to time ejected through the pylorus, sometimes being accompanied by some of the undigested food; but this does not generally begin to occur until one or two hours after digestion has begun. But it would be impossible, with our present knowledge, to say exactly how long food remains in a healthy stomach, or how much of the digested materials are absorbed there. As we have seen (in 1) there are, however, many reasons for believing that the peptones are in great part absorbed, or at least leave the stomach soon after they are formed, and the future peptonization consequently greatly favored. The chyme contains some peptone, as well as the unabsorbed products of the uncompleted digestion of the albumen, as nitrogenous matter in a dissolved and in a finely divided form in a state of suspension; there may be present also other bodies that have undergone little or no digestion, such as epitheliums, fats, cellulose, starch, etc. Its reaction is acid, but after its arrival in the intestine and its admixture there with the bile and pancreatic juice the acidity is lessened, until in the jejunum it becomes freely alkaline, a reaction that the intestinal contents continue to present till an acid fermentation is set up in the cæcum. But if admixture with the bile does not at once neutralize the acid of chyme, it immediately precipitates the pepsin and part of the peptones contained in it.

Theories as to the Nature of the Digestive Action of the Gastric Juice.—1. That it acts like very dilute hydrochloric acid, the pepsin merely hastening the process. 2. SCHMIDT regards the pepsin and the hydrochloric acid as being loosely combined, and believes that in the process of digestion this pepto-hydrochloric acid unites with the albuminous bodies. 3. MEISSNER was of opinion that in the digestion of proteids two bodies are formed—the peptones, readily assimilable, and a peculiar parapeptone that requires subsequent modification before being absorbed. HAMMARSTEN, on the other hand, states that pure pepsin transforms egg albumen entirely into peptones, without giving a trace of parapeptone. This parapeptone of MEISSNER corresponds to the antialbumate which KÜHNE asserts makes its appearance with an imperfect digesting fluid. MEISSNER also described a series of peptones differing slightly one from the other, which he said were formed in the process. 4. That the acid softens and swells the proteid, while the pepsin, acting as a ferment, chymifies, the process most probably being one of hydration, possibly even originating in the simple splitting up of the larger proteid molecules. On this view the albumens may be regarded more or less as anhydrides, and the peptones as hydrates. It does not appear that a simultaneous action of the acid and the pepsin is necessary, for if finely divided fibrin is digested for some time with a dilute solution of pepsin, then washed with water, and digested at 38° for two days with hydrochloric acid (0·4 per cent.), it dissolves almost completely. The liquid, when mixed with an equal volume of alcohol and filtered, yields a solution of peptone not precipitated by nitric acid. The pepsin would thus appear to combine, in an insoluble form, with certain albuminoid substances, so modifying them that they undergo hydration in pure water at 40° with the formation of true peptones (WURTZ).

According to BRÜCKE the proteid is first converted into syntonin, and this subsequently into peptone. KÜHNE regards every natural proteid as consisting of a combination of two residues of an *anti-* group and *hemi-* group, into which it may be split by the action of gastric or pancreatic juice; that these bodies are further respectively converted into an *antipeptone* and a *hemipeptone*, these bodies being preceded, however, by the formation of syntonin-like substances, *anti-* and *hemi-albumose.* But in pancreatic digestion the hemipeptones may undergo even further change and be partly converted into leucin and tyrosin.

Peptic Digestion.

Albumen
containing a *hemi-* and an *anti-* residue.

Antialbumose.	Hemialbumose.
Antipeptone.	Hemipeptone (part of which is broken down into leucin and tyrosin in pancreatic digestion).

Kühne's antialbuminate (Meissner's parapeptone) is a body that makes its appearance when dilute hydrochloric acid alone, or pepsin in an imperfectly active condition or in insufficient quantity, is used in the albumen digestion. It can be changed into peptone by the pancreatic, but not by the gastric juice. *Antialbumid* (hemiprotein, dyspeptone) is derived from the antialbumate by the action of dilute hydrochloric acid.

Dilute Hydrochloric Acid (¼ per cent.) at 40°.

Albumen.

Antialbumate.	Hemialbumose.
Antialbumid.	Hemipeptone (which is further broken down into leucin and tyrosin by the action of dilute sulphuric acid, 3 to 5 per cent.)

The action, then, of the gastric as well as of the pancreatic juice, according to the weight of evidence, is double and successive, the albuminoid bodies being first converted into a substance variously named, and corresponding to an acid albumen, albuminose, or syntonin, and then into peptone.

Histological Changes in the Secreting Cells as the Result of their Activity.—This very interesting subject can of course be only very generally referred to here. In the mucous membrane of the stomach is a closely packed series of tubular glands. These are of two kinds, in one of which there is a continuous lining of epithelial cells around the central lumen, and which may accordingly be called *central cells;* and in the other, in addition to these central cells, some large ovoid or, as they have been termed, *peptic* cells are also present, peripherally situated. It used to be taught that the former variety of tubular glands, which are in greatest numbers towards the pylorus, merely secreted mucus, or assisted in the absorption of the digested proteids; while the latter, in which the so-called peptic cells are present, and which are most numerous in the cardiac end of the stomach, were described as secreting the gastric juice, the central cells near the mouths of the tubes furnishing the acid and the large peripheral ovoid cells the pepsin. It would now appear that *all these gastric glands* secrete a pepsigenous juice, the central cells, however, being the pepsin-formers and the large ovoid peripheral cells secreting the free acid (HEIDENHAIN).

The following is a summary of some of the chief changes that occur in these secreting cells not only in the stomach but also in the pancreas:—

(*a*) *Stomach.*—*The central cells* of the gastric tubular glands are pale and finely granular *in a state of rest*, and do not stain readily in carmine, etc. When these cells are large and bright they contain much pepsin material, but comparatively little when shrunk and turbid. *In a state of activity* they are swollen, turbid, and coarsely granular, and stain readily; becoming after a time smaller, but more turbid and granular than at first, and staining more deeply.

The ovoid or peptic (?) cells are also swollen during digestion, but appear otherwise unchanged. They are stained by carmine, and only swell up in hydrochloric acid (1 per cent.) at 40°, not being digested by it, as is the case with the central cells. In the pancreas the granular part of the cell does not stain readily, and the granules that accumulate in the resting condition disappear when the cell is active; on the contrary, in the central cell of the peptic glands the granules increase with the increased activity of the gland, and it is then that the deepest staining can be obtained.

(*b*) *Pancreas.*—The secreting cells of the glandular acini have the form of short cylinders, in which two zones are generally to be distinguished, an inner, next the lumen, which has a *granular*, cloudy appearance, and an outer, of a *homogeneous* or finely striated aspect, and readily stained by carmine, the nucleus lying more or less intermediate. The size of these two zones varies according to the condition of digestion, for after a state of activity the inner granular zone becomes narrow and sometimes disappears, appearing to furnish material for the secretion, and being renewed at the expense of the outer zone, which in turn is maintained at the expense of the blood. The amount of the zymogen rises and sinks with the granular inner zone (HEIDENHAIN). In a state of *hunger* this zone is the more conspicuous, the outer homogeneous zone being insignificant. In the *early stage of digestion*, some hours after the taking of food, the cells undergo a decrease in size, owing to the consumption of the granular zone, the homogeneous zone, however, showing an increase. At a *later stage* the secretion sinks, and the granular zone becomes built up anew at the expense of the homogeneous outer zone, and this latter is reduced to a minimum. *After long starvation* the homogeneous zone is the more abundant, the inner zone being much reduced.

Conditions Affecting the Digestive Phenomena.—The action of the pepsin on the albumen is *dependent on the temperature* and on the *proportion of pepsin and of free acid present.* The most suitable temperature seems to be about 37°, as above 50° the juice begins to lose its digestive properties and above 60° becomes inert; at 0° it also loses its activity, but it recovers it again on being heated. It is probable that the digestion of fibrin begins quicker and continues more rapidly the greater the proportion of pepsin present. A proportion of

0·8 to 1 gram hydrochloric acid per litre makes a fairly digestive fluid; but for cooked albumen a proportion of 0·17 per cent. acts most strongly, although **Ebstein** and **Grünster** found 0·2 per cent. the most useful strength. Pepsin seems to act best when the acid present bears a definite relation to the albumen molecule with which it probably enters into combination. Accordingly the process of conversion uses up the free acid, while it does not appear directly to involve any destruction of the pepsin. A very small quantity of pepsin may therefore effect the conversion of a very large amount of albumen.

In some experiments of **Brücke's** *upon the rapidity of digestion in relation to the amount of pepsin and acid present*, he found that when a 0·1 per cent. hydrochloric acid was used in the digestion of fibrin the conversion went on more rapidly with an increased proportion of pepsin; with x pepsin, for example, the digestion was completed in forty-five minutes, with $2x$ in twenty minutes, with $4x$ in fifteen minutes, and with $8x$ in ten minutes. An increase in the percentage of the acid, on the other hand, rendered the digestion much slower, about one hour being added for every $\frac{1}{10}$ per cent. of acid above $\frac{1}{10}$ per cent. But some definite relationship seems to exist between the relative amounts of acid and pepsin in a good digestive liquid, for we find that dilute pepsin solutions act best with dilute acid solutions, while strong pepsin solutions require a greater proportion of acid. Fibrin is said to need a less degree of acidity for its digestion than white of egg.

The quantity of water present also affects the process, much water retarding it. An accumulation of the peptonized albumen mechanically hinders its continuance; the presence of bile also interferes; and so likewise is the case with acetate of lead and mercuric chloride, except in very moderate quantity, concentrated solutions of sodic chloride and of the alkalies, dilute solutions of phenol, and alcohol in excess—they all interfere more or less with the digestive process in the stomach, chiefly by precipitating the pepsin or the peptones, or by causing a copious alkaline exudation. Beer does not appear to act detrimentally (**Bucheim**); and spices, such as ginger, pepper, and cinnamon, appear to encourage the secretion of the juice.

The properties of the peptones have already been given (p. 119), also their modes of preparation (pp. 119, 150).

To purify them, neutralize the acid liquor containing them with baric or calcic carbonate; then boil, concentrate over a water bath, and filter. To purify still further recourse may be had to dialysing the solution, but the process is very slow; instead we may separate excess of baryta by the careful addition of sulphuric acid and subsequent filtration; or if lime has to be separated, first concentrate by evaporation and then precipitate with alcohol; a little lime, however, remains combined with the peptone.

The secretion of the gastric juice is essentially intermittent, and is excited by different stimuli. Different bodies introduced into the stomach cause the mucous membrane to become red and swell up, and subsequently to pour out its secretion; the character of the stimuli is said to affect the character of the secretion, that excited by mechanical or chemical excitation being less rich in digestive principles (pepsin, etc.) than that secreted under the influence of the food; the degree of acidity probably also varying with the nature of the physiological stimulus. This secretion is probably the result of a direct irritation of a local ganglionic centre that is in connection with the central nervous system. Afferent impulses likewise pass up the vagus, and by inhibiting the vasomotor centre in the medulla bring about the dilatation of the vessels of the stomach, section of the vagi leading to a temporary anæmia of the mucous membrane (RUTHERFORD).

Pepsin is possibly formed more or less continuously in the glands, although it is not probably contained there in a free state, but rather as an albuminate combination that is easily split up and rendered active by hydrochloric acid or a chloride. The *hydrochloric acid* appears to be formed only as the result of reflex or direct stimuli; but while in the fundus free acid is present, being secreted there, this does not seem to be the case in the pyloric end. A mucous membrane rich in pepsin also contains much sodic chloride (0·6 to 1·5 per cent.) In the formation of free hydrochloric acid a dissociation process probably precedes in the chloride, $2Na_2HPO_4 + 3CaCl = Ca_32PO_4 + 4NaCl + 2HCl$ (MALY). THUDICHUM assumes that sodic chloride and lactate are split up in the walls of the stomach into free acid and caustic soda, $NaCl + H_2O = NaHO + HCl$. This caustic soda according to THUDICHUM, assists in protecting the mucous membrane of the stomach against the action of the gastric juice, and becoming converted into carbonate enters the blood and is carried to the liver; but the continuous circulation of alkaline blood through the mucous membrane of the stomach is no doubt one of the reasons why it is not digested (PAVY); the question, notwithstanding, cannot yet be regarded as solved.

The pepsin is poured out abundantly on the taking of food, then falls in amount for the next hour or two, and rises again about the fourth or fifth hour (GRÜTZNER). Its secretion appears to be favored by the previous ingestion of dextrin and certain other pepsigenous materials (SCHIFF).

Pathology.—The amount of pepsin as well as of the whole juice, appears to be much reduced in fevers and acute anæmia; in some of these cases, as well as occasionally in catarrh of the stomach, pepsin and hydrochloric acid may be both absent; but we may find instead butyric or lactic acids in greater or less quantity.

Sarcinæ, bacteria, and different fermentation products may at times present themselves; also mucus in excess, and bile, and in *hæmatemesis* blood, which last may be vomited up unaltered, or, if it has lain some time in the stomach, in the form of dark coffee grounds. The vomit may be alkaline and contain albumen, epithelium, and mucus, as in cholera; or urea, carbonate of ammonia, etc., as in uræmia, etc.

Digestion is interfered with by the presence of bile or mucus, much free acid or alkali, much metallic salt, chlorides, sulphates, or nitrates, anhydrous salts hindering fermentation more than hydrous salts; the alkaloids also, except quinine, retard the process.

As to *gases in the stomach*, normally little or none is present with the exception of the air that has been swallowed with the food or of a little that has diffused from the blood; for the gases resulting from fermentation will not be met with unless some abnormal condition is set up, although it is possible for some of the gas occasionally found on the stomach to come up from the duodenum.

Planer found gases having this composition:—

CO_2=20 to 33 per cent.
H = 7 " 27 "
N =38 " 72 "
O = 0·4 "

and Hofmann and Ewald:—

CO_2= 1·7 to 28 per cent.
H =20 " 32 "
CH_4= 0·2 " 10 "
O = 6 " 11 "
C_2H_4 and N, traces.

Owing to the diminution in the hydrochloric acid in fevers, and to the tendency of the mucous membrane of the stomach to become catarrhal, decomposition processes are favored, and the digestion greatly interfered with. In some of these cases the pepsin does not appear to be wanting, rather the acid to set it free and render it active.

CHAPTER VIII.

PANCREATIC JUICE.

This is a clear, odorless, and very alkaline liquid (= 0·3 per cent. Na_2CO_3), having a salt taste and a specific gravity of 1008 to 1010; it is ropy and viscid when first collected, but later it becomes thinner. It decomposes readily. When heated to 75° a slight coagulum appears, which likewise occurs on the addition of alcohol, mineral acids, tannic acid, metallic salts, magnesic sulphate, and chlorine water.

Quantity.—From researches on dogs the amount secreted in the twenty-four hours has been estimated at 150 grams (5¼ oz.) (Bidder and Schmidt), or 140·7 grams (Ludwig and Weinmann); but it is more probable that it amounts on an average to 10 or 11 oz.

The Secretion.—Immediately after food is taken its secretion begins, reaching its maximum two hours later; then occurs a fall, succeeded by a secondary rise some five or six hours afterwards, and a sinking again to zero in sixteen to eighteen hours, but rising again rapidly with fresh ingestion of food (Bernstein). The secretion appears to be most active five to seven hours after a meal.

Nausea or vomiting and section of the vagus stops its secretion temporarily; and it is increased by stimulation of the medulla oblongata, or by centripetal stimulation of the vagus.

Its Chemical Constituents are water, albumen, mucin, fats, ferments, and salts, the last consisting chiefly of sodic and potassic chlorides, calcic phosphate, sodic carbonate, and traces of ferric phosphate. Fresh juice contains bodies similar to salivary corpuscles, and only traces of leucin, neither peptones nor tyrosin being present (Kühne).

After the juice has stood some time tyrosin, fats, and a small amount of soaps may also make their appearance, the leucin and tyrosin being due probably to an intrinsic digestion of the albumen of the juice itself. A comparatively large amount of soda is present, peculiarly associated with the albumen, and probably in the form of carbonate, to which the alkaline reaction of the juice is due.

Analysis of Pancreatic Juice—Dog (C. Schmidt).

	From a permanent fistula.	From a freshly opened pancreatic duct.
Water	98·08	90·07
Solids	1·92	9·93
Organic substances, as albumen, alkali albumen	1·26	9·04
Inorganic salts	0·66	0·89
Soda combined with albumen, and traces of lime and magnesia similarly combined	0·33	0·09
Sodium chloride	0·24	0·73
Potassium	0·08	0·02
Phosphates of lime, magnesia, and soda	0·01	0·05

The normal pancreatic juice contains, according to Bernard, from eight to ten per cent. of solids, of which about one per cent. consists of inorganic salts and the rest of organic matters: this corresponds with Schmidt's analysis of a normal juice obtained from a recent fistula. The juice coming away from a permanent fistula soon alters in character, and accordingly is not a correct representative of the normal secretion, being much thinner, and containing much carbonic acid, and only about one to two per cent. of solids; guanine ($C_5H_5N_5O$) has also been found in it. But Bernstein only obtained an average of 3·3 per cent. solids in an apparently perfectly normal juice, of which 0·8 per cent. was inorganic matter. The above estimates, it should be said, apply chiefly to the secretion in dogs.

The *pancreatic peptones* are precipitated by acids and acid salts, except the acid phosphate of soda, and the filtered liquor is precipitated by tannic acid and acetate of lead (Diakonow), thus differing from gastric peptones.

Ferments.—1. *A diastatic ferment,* isolated by Cohnheim and Wittich, and probably identical in many respects with ptyalin; it rapidly changes starches into sugars.

2. *A peptone-forming ferment, pancreatin or trypsin.* After long fasting this ferment is absent (Hertzen).

3. *A ferment which splits fats by hydration into fatty acids and glycerin.* It has not yet been isolated.

Zymogen.—According to Heidenhain there is no preformed free ferment in the pancreas, but there is present in the gland a body he names *zymogen*, which builds up one or more of these ferments. From this zymogen, naturally after each act of stomach digestion, and artificially by treatment with acids, the ferments are obtained for the digestion of albumens, and probably also for that of the starches and fats. These ferments are active in alkaline and neutral fluids; a temperature above 50°, as also the addition of alcohol in excess, destroys or hinders their activity, although *dry* trypsin may be heated up to 110° without losing its ferment power. Pepsin also appears to act deleteriously, rendering trypsin inactive, but this is not apparently the case with the zymogen.

The varied action, then, of the pancreatic secretion depends on the presence of these three ferments. They are collectively more soluble in solutions of sodic chloride, alkaline sulphates, and potassic chlorate than in water. The *albumen ferment* is soluble in sodic hyposulphite, potassic arsenite, and tartaric acid; the *diastatic* ferment specially soluble in potassic arseniate and tartaric acid; and the *fat ferment* in a mixture of bicarbonate of soda with one-fourth its volume of caustic soda solution, or in antimoniate of potash. By means of these solvents a separation may be effected of the different ferments, dialysing at the same time through porous earthenware under reduced pressure (PASCHUTIN).

The zymogen is soluble in water, where it is readily split up, after exposure for some time to the air, into trypsin, etc., but little or none of the ferments is dissolved out of the gland substance by glycerin, unless the zymogen has been previously decomposed by the action of dilute acids or otherwise. The decomposition of the watery solution occurs more readily at an elevated temperature and under the action of acids, and it is more or less hindered by the presence of soda or its carbonate; but the ferment, when once formed, is more active in presence of soda or sodic chloride than in a simple watery solution.

The *amount of zymogen in the gland* depends on the condition of the digestion, being most abundant fourteen to twenty-four hours after food, although the juice richest in the albumen ferment is generally secreted six to nine hours after a meal; and it is probable that a constant formation of zymogen is going on in the secreting cells, and that at intervals, under the influence of certain stimuli, this zymogen is converted into the pancreatic ferments, which, as we have seen, are the products of the secretion of the inner zone of the secreting cells of the pancreas.

The separation of the *pancreatin* from the fresh gland can readily be effected by rubbing up the gland with 1 per cent. acetic acid, in the proportion of 1 gram gland substance to 1 c.c. acetic acid, and then digesting for several days with glycerin. A watery solution acts very slowly, but the presence of sodic chloride, or better still of soda, quickens its action. The more ferment is present the less soda is necessary; but with a moderate amount of ferment a percentage of 0·9 to 1·2 of soda is most favorable. With 6 per cent. soda the action is much hindered. It acts properly only in neutral or weakly alkaline fluids, and without any previous swelling up of the fibrin or coagulation of the albumen immersed in it, such as occurs in gastric digestion.

The *diastatic ferment*, while apparently identical with the ptyalin of saliva, appears to be more active in its properties.

The *fat ferment* has not yet been isolated, but an active extract can be obtained by rubbing up some quite fresh pancreas with a mixture of glycerin (nine parts) and soda solution (1 per cent. one part) together with some clean sand, and allowing the whole to digest for four days. Acids destroy the action of this ferment.

As to the activity of these ferments, it would appear that their action within certain limits is in inverse proportion, a double quantity doing a given amount of work in half the time; further that they liberate their energy at a progressively retarded rate (W. ROBERTS).

It follows therefore from the above that the *digestive actions of pancreatic juice* may be classified under these heads:—

1. It *changes starches rapidly into grape sugar*, acting more powerfully than saliva; the transformation is very rapid at 35°, and the presence of bile or gastric juice does not retard its action. One gram of the juice of a dog, containing only 0·014 gram of organic solids, converted 4·672 grams of starch into sugar and dextrin in half an hour at 35° (KRÖGER). Not till the second month after birth is the infant's pancreatic juice able to digest starch, but at the age of a year its power in this respect is equal to that of the adult.

2. *It dissolves coagulated albumens*, acting best at 35° to 40°, *changing them into peptones*, appearing to act specially on muscle fibre and fibrin; but its general action on albuminoids is nearly ten times more energetic than that of gastric juice. Gelatins are also converted into peptones, and with prolonged digestion leucin and much glycocin may appear. By the action of alkaline solutions of pancreatin on albumens DANILEWSKY in some recent researches obtained several intermediate bodies, but the final product was always peptone. An albumen is first produced insoluble in water and warm alcohol, of weak acid reaction, and containing sulphur together with lime and phosphorus. The bodies next formed are more soluble in water and warm alcohol, more strongly acid, and free from lime and phosphorus. Finally come the peptones, which combine with bases and acids and yield no sulphide with alkalies.

The undigested proteids issuing from the stomach are to be digested entirely or in great part by the pancreatic juice, and the presence of bile favors rather than hinders the process; but to what stage the digestion is carried, and whether much of the peptones formed is broken down into leucin and tyrosin, etc., is unknown. Further and later decomposition products of these peptones may appear, such as aspartic and glutamic acids, and even xanthin and hypoxanthin (RADZIEJEWSKY, SALOMON).

From *prolonged action* of this juice outside the body, but more probably also as a result of decompositions occurring (KÜHNE), certain other products may show themselves, such as indol, skatol, phenol, phenyl-sulphuric, phenyl-acetic, and phenyl-propionic acids.

3. *It contributes very largely to the digestion of fats*, emulsifying and also saponifying them to a slight extent—the latter possibly, however, only so far as to facilitate the emulsifying of neutral fats. The emulsifying property is not entirely due to the alkalinity of the juice (BERNARD), but is probably in great measure dependent on the alkali albumen present.

In experiments with pancreatic juice great care should be taken that it is *prepared from a fresh and unaltered gland;* otherwise imperfect results will be obtained. As an example how readily the character of the secretion is altered, it is stated that the removal of the spleen deprives the pancreas of peptone-forming power (SCHIFF). It is very difficult also to avoid decompositions occurring in experimenting with pancreatic extracts, bacteria soon making their appearance unless such a body as salicylic acid is added.

Difference between Peptic and Tryptic Digestion.—Pancreatic digestion, it should be noted, includes the action of the three ferments, tryptic being applied solely to the albuminoid conversions and changes.

1. Peptic digestion only occurs in an acid medium; in pancreatic the reaction is alkaline, and some alkali must be present for it to take place: the acidity of the gastric juice, represented by 0·2 per cent. hydrochloric acid, is in the pancreatic juice replaced by an alkalinity corresponding nearly to 1 per cent. sodic carbonate.
2. In tryptic digestion a globulin body resembling alkali instead of acid albumen is formed previous to the peptone stage.
3. A considerable amount of proteid in tryptic digestion is broken down beyond the peptone stage into leucin and tyrosin, the antipeptone residue, however, which forms about half the weight, resisting this decomposition.
4. While fibrin is readily acted on by both juices, boiled albumen and syntonin are more easily converted by the gastric than by the pancreatic secretion.
5. In the case of fibrin, with tryptic digestion, no previous swelling up occurs, as in gastric digestion, and it remains opaque, appearing to be corroded rather than dissolved. Indeed, in alkaline tryptic digestion albuminous bodies generally undergo no previous swelling up or coagulation, as is the case with peptic digestion.
6. Pancreatic juice does not appear to have any direct solvent action on the gelatiniferous elements of the tissues, unless these have previously been boiled or treated with acids.
7. Trypsin dissolves mucin, which is unacted on by pepsin.
8. Decomposition sets in readily during pancreatic, but very slowly during gastric digestion.
9. In gastric digestion the rotatory power of the transformed matter is but little lessened, remains unchanged, or is increased, whilst in pancreatic digestion it is always enormously lowered (BÉCHAMP).

Pathology.—In certain diseases of the pancreas, such as chronic inflammation, degeneration, and cancer, a great excess of fatty matters appears in the evacuations.

Pancreatic calculi are occasionally, but rarely, met with; they are like salivary calculi, and consist chiefly of phosphate of lime (60 to 80 per cent.), a little carbonate of lime (10 to 20 per cent.), and animal matter (7 to 16 per cent.)

CHAPTER IX.

INTESTINAL JUICE.

THIS juice is a clear, opalescent, greenish yellow, and stongly alkaline viscid secretion, having a specific gravity of 1011 (THIRY), and containing about 2·27 to 2·4 per cent. of solids, of which more than one-third consists of inorganic salts, one-third albumen, and less than one-third of the other organic bodies. It effervesces with acids, yields no mucin, and is coagulated by alkaline chlorides and sulphates in excess.

It appears only to be periodically secreted, and is a mixture of the secretions of Brunner's glands and Lieberkühn's crypts. Comparatively little is known as to its exact composition and properties, some even regarding the fluid obtained by THIRY'S process as more or less of a transudation.

Quantity.—From the amount secreted by a small piece of the intestine of a dog, THIRY calculated that the whole small intestine secreted, from the second to the fifth hour after a meal, 360 grams (12¾ oz.) of intestinal juice. BIDDER and SCHMIDT'S estimate was 300 c.c., or 10⅖ oz.

	Dog (THIRY).	Horse (COLIN).
Water	97·58	98·10
Solids	2·41	1·80
Albumens	0·80	0·45
Other organic constituents . .	0·73	
Inorganic salts	0·88	—
Carbonate of soda	0·32	1·45

A paralytic secretion has been obtained which is clear, yellowish, strongly alkaline, specific gravity 1008, poorer in solids than the normal juice, and containing only about a quarter as much organic, but nearly the same amount of inorganic constituents; it also contains about 0·016 per cent. urea.

Actions.—It is probable that some of the diversity of opinion as to the action of this juice is due to a difference in the character of the secretion in different animals. Thus the intestinal juice of dogs, pigs, and rabbits converts cane into grape sugar, but this is not so with the juice of ruminants, etc.

1. It probably contains a diastatic ferment, soluble in sodic nitrate and potassic and sodic bicarbonate, capable of readily converting starch into sugar (COLIN, SCHIFF), although this is denied by THIRY. But a glycerin extract of the whole mucous membrane of the small intestine undoubtedly contains a diastatic ferment capable of converting starch into sugar.

2. It contains a ferment soluble in potassic chlorate, which converts cane into grape sugar, transforming some of the latter into lactic and butyric acids (FRERICHS); but a little of the cane sugar remains unchanged (HOPPE SEYLER).

3. Its actions on fats is doubtful, probably negative (THIRY). It may, however, exert a slight emulsifying action (SCHIFF).

4. It appears that fibrin is rapidly dissolved by it (THIRY, KÜHNE), and probably also a little casein and albumen (SCHIFF). The fibrin does not swell up, but crumbles to pieces. Accompanying this peptonization, if not the cause of it, there seems to be a certain amount of decomposition of the proteid.

5. Cellulose, gums, etc., are not necessarily modified.

Further, in the intestinal digestion certain ferments play a part by producing diastases that superimpose their own digestive actions on those set up by the organic diastases. Neither the diastases of the ferments nor those of the organism ever cause a disengagement of gas, and the carbonic anhydride and hydrogenated gases formed in the intestine must be attributed to the microbes living therein (DUCLAUX).

As to the *secretion of Brunner's glands* we know little, but it is stated that an extract of the gland digests fibrin in an acid solution (GRÜTZNER); COSTA states that these glands yield mucin, and RABUTEAU and LEVEN that its reaction is acid. Brunner's glands are related structurally to the pyloric glands of the stomach, and as the latter possess a peptogenous power (HEIDENHAIN), possibly they are likewise related in function.

The surface cells also of the duodenum near the pylorus are said to contain pepsin.

BUDGE and KROLOW found that a watery extract of Brunner's glands converted starch into dextrin and sugar, and fibrin into peptone.

Iodides, bromides, sulphocyanides, and lithia salts absorbed in the stomach appear again in the small intestine (QUINCKE).

The secretion obtained from the large intestine is mucous, viscid, alkaline, and contains very little albumen; it is said to possess the power of converting starch into sugar, but it apparently exercises no solvent action on albumens or fats.

CHAPTER X.

THE BILE.

Physical Properties.—When the bile flows from the liver it is clear and syrupy, of a golden brownish yellow color (greenish in herbivora), having a sweetish bitter taste, a specific gravity of 1009 to 1020, and a neutral or weakly alkaline reaction (but slightly acid in the carnivora). After having lain some time in the gall bladder the bile becomes concentrated, has a sour smell, is darker in color, charged with mucus, and may contain particles of fat and calcic phosphate.

Absorption Spectrum.—Perfectly fresh normal bile gives no absorption bands, although ox gall, even when fresh, is said to give a band between D and E; but when the bile has altered, as by standing for some time, or when an alcoholic extract is used, it becomes dichroic, green in thin and red in thick layers, also altering in color through green and blue to a reddish tint, and shows four absorption bands—one in front of C, one on each side of D, and one before E, only the middle two being dark and sharply defined.

Amount.—Very various estimates have been given, but the average may be taken as 1,000 to 1,700 grams (2·2 to 3·7 lbs.) in the twenty-four hours. NASSE estimated it at 45 to 47 oz. for a man of 142 lbs. weight, RANKE at 23 oz. for a man of 104 lbs., and WITTICH obtained nearly the same result in a woman with a biliary fistula, the bile of the twenty-four hours containing about $\frac{4}{7}$ oz. of solids and averaging about 2·2 per cent. of the body weight.

Secretion.—The liver receives a large amount of blood, which is especially abundant during digestion, although it is comparatively poor in oxygen, yet rich in materials absorbed from the alimentary canal.

The secretion of bile is continuous, but it becomes more active two hours or so after a meal, and this activity continues to increase for the following five to seven hours, but then diminishes rapidly. According to BERNARD the maximum period is seven hours after, but authorities differ. The pressure under which it is secreted is very low, and accordingly its flow is easily obstructed. But although secreted continuously with varying rapidity it is only discharged into the intestine at intervals as required, an accumulation occurring in the gall bladder.

The passage of the acid chyme from the stomach over the orifice of the bile duct acts as a reflex stimulus to the contraction of the gall bladder, and to a consequent outpouring of the bile.

Chemical Composition.—The three important constituents of the bile are the biliary acids, the biliary pigments, and the cholesterin, but the two former are the most characteristic. In addition we find lecithin, cholin, fats, soaps, a diastatic ferment in small amount, and different salts.

Human Bile (FRERICHS, GORUP BESANEZ, etc.)

	Per cent.
Water	86 to 90
Solids	14 " 10
Biliary acids and salts	5·6 " 10
Fats	0·3 " 1·7
Cholesterin	0·4 " 1·0
Mucus and Pigments	1·4 " 2·9
Mineral salts	0·6 " 1·0

Solids in Human Bile.—The amount of solids in the bile obtained from dead bodies is much greater than that contained in bile flowing away from a fistula; in the latter the solids form only 1·2 to 2·3 per cent., while in the former they are as high as 10 to 14 per cent. It is very probable, however, that this is nearer the normal condition than is the case with the fluid discharged by an open fistula.

In *post-mortem* bile HOPPE SEYLER obtained—

	Per cent.
Glycocholate of soda	3·03
Taurocholate "	0·87
(containing sulphur	0·05)
Soaps	1·39
Mucin	1·29
Lecithin	0·53
Cholesterin	0·35
Other organic substances insoluble in alcohol	0·14
Iron, probably as phosphate	0·006

In 100 parts dry solids of bile *obtained from a fistula*, having a specific gravity of 1010 and 2·24 to 2·28 per cent. of solids, JACOBSEN got—

Glycocholate of soda	44·8
Sodic chloride	24·5
Palmitate and stearate of soda	6·4
Phosphate of soda	5·9
Carbonate "	4·2
Cholesterin	2·5
Phosphate of lime	1·6
Potassic chloride	1·2
Lecithin	0·2
Fats	0·4
Residue insoluble in alcohol and ether	8·1

In this analysis **Jacobsen** found no sulphur, but in several other analyses he obtained a large percentage of this body, pointing to the presence of much taurocholate of soda (so also **Bischoff**). A variation in the relative proportions of these two biliary acids is possibly produced by the character of the food. Indeed, **Jacobsen** has not found the composition of human bile to be very constant, the biliary acids varying from 3·9 to 10·8 per cent., and the specific gravity, which generally averages 1017, may be as low as 1010.

The percentage of sulphur in bile varies between 1·88 and 3·41, and of nitrogen between 7·23 and 10·66 (**Spiro**).

In fuller detail the *chief constituents* may be said to be—

1. *Resinous acids*, the so-called biliary acids, which exist in the bile as soluble alkaline salts; for example, glycocholate of soda, $C_{26}H_{42}NaNO_6$. Of the two biliary acids most modern analyses indicate the glycocholic as preponderating in human bile. The mean of six analyses gave a percentage of 6·47 biliary acids, of which the taurocholic formed 1·56 per cent., containing 0·09 per cent. of sulphur (**Jacobsen**).

2. *Pigments*—bilirubin, biliverdin, and sometimes bilifuscin.

3. *Mucin.*

4. *Cholesterin.* This is maintained in solution by the taurocholate of soda. It is stated to form 1·6 per cent. in human bile (**Flint**), and is probably one of the decomposition products of nerve substance.

5. *Lecithin*; probably *cholin* or *neurin*, an alkaline basic derivative of the lecithin; a small quantity of urea, and of fats existing chiefly as alkaline soaps.

6. *The mineral constituents* are formed chiefly by sodic chloride, which with soda salts constitutes over three-fourths of the ash of bile; there are also alkaline salts of the fatty acids, and phosphates of lime, magnesia, and iron.

7. *Gases.* The bile contains a large amount of gases, partly dissolved in and partly combined with it. In the rabbit the freshly secreted bile contains an average of 109 per cent. carbonic acid, and in the dog about 57 per cent.; only traces of oxygen and nitrogen are present (**J. J. Charles**).

In some animals a diastatic ferment has been obtained from the bile. In adult men the bile is poorer in water and fats, and richer in biliary acids, pigments, mucus, and mineral salts than in women and children; no proteids are present under normal conditions.

In ox bile taurocholate and glycocholate of soda are present, in sheep's bile the taurocholate preponderates, and this is the only acid present in dog's bile, while in the bile of pigs we find hyoglycocholate and hyotaurocholate of soda ($C_{27}H_{43}NO_5$ and $C_{27}H_{45}NSO_6$).

Effect of Food, etc.—Abstinence lessens the amount of bile formed; with a fatty diet little bile is secreted, but more with a diet of bread and rice; a rich nitrogenous diet increases the amount as well as the solid constituents, but a good mixed diet (as bread and meat) seems to be the most effective (**Wolfe**).

The composition of the bile, besides being affected by the character of the food, is also influenced by the period of its secretion, the acids appearing to be increased during digestion, then diminished in amount, and increased again after several hours (**Hoppe Seyler**).

Watery solutions of the biliary acids injected into the blood increase the biliary acids in the bile (**Huppert**); the same effect is likewise produced by injecting bile into the small intestine (**Schiff**). An increase of the pigments occurs after the injection of oxyhæmoglobin or bilirubin solutions into the blood (**Tarchanoff**).

Action of the Human Bile.—1. *Emulsifies fats* to a slight degree; also *dissolves them slightly*, particularly the three fatty acids, both saponifying and emulsifying, especially in presence of pancreatic juice.

2. *Aids in the absorption of fats*, as membranes moistened with bile admit the passage of fats more readily. In chyle, for instance, which normally contains 3·2 per cent. of fats, the proportion is reduced to 0·2 per cent. when the flow of bile into the intestine is stopped.

3. *Checks putrid fermentations* and acts as a natural stimulant to the intestinal mucous membrane. The biliary acids are powerful antiseptics, especially the taurocholic (MALY, EMICH).

4. *The bile precipitates all the pepsin in the chyme entering* the small intestine, and if the chyme is neutralized or rendered even slightly alkaline peptones or syntonins will also be precipitated. The pepsin, which would interfere with the action of the trypsin, is thus disposed of. The partially digested food passing from the stomach is accordingly well prepared for the action of the pancreatic and intestinal juices, the presence of bile, so detrimental to gastric digestion, rather favoring the action of these juices.

In some animals bile converts starch into sugar.

Rôle of the Bile in the Economy.—In addition to assisting in the digestion of the fats the bile also serves to excrete different decomposition products from the system. The greater part of the biliary acids is reabsorbed and further oxidized, the intermediate products between them and carbonic anhydride and water being unknown; the remaining portion is decomposed and excreted. Excreta and vomited matters sometimes, but particulary in diseased conditions, may contain traces of the biliary acids, but their decomposition products (as cholic and choloidic acids and dyslysin) are more likely to be found than themselves. The pigments are reabsorbed in part, and in part also, together with the cholesterin, excreted in the fæces.

But it is very probable that several of the ingredients of the bile are repeatedly absorbed and re-excreted during the process of digestion.

Source and Production of the Biliary Constituents.—*The biliary acids* are not met with in the blood, although glycocin and taurin, albumen derivatives, are possible constituents of parts of the organism; these acids (or at least cholic acid) are secreted by the hepatic cells, at the expense probably of an albuminoid, the nitrogen radicle being derived therefrom, while the cholic acid radicle may be derived from the fats, the combination of the two being effected in the liver. Among the decomposition products of cholic acid lauric and stearic acids have been obtained (TAPPEINER).

Some of the hæmoglobin as well as of the fibrin disappear from the blood in its passage through the liver, and the bilirubin is possibly indirectly derived from the former.

Hæmatoidin, $C_{30}H_{34}N_4O_6$;
Hæmatin, $C_{32}H_{34}FeN_4O_6$;
Bilirubin, $C_{32}H_{36}N_4O_6$.

Its source is regarded as the hæmoglobin of the blood that is broken down in its passage through the liver. The injection into the blood of solutions of bodies capable of dissolving the colored corpuscles, and thus setting free the hæmoglobin, has been found to cause bile pigments to appear in the urine

Tarchanoff obtained an increased discharge of the bile pigment by injecting bilirubin or oxyhæmoglobin into the veins of a dog. But the spectra of hæmatoidin and bilirubin are quite distinct (Preyer). We cannot do more, therefore, with our present knowledge, than regard the above hypothesis as to the origin of bilirubin as probable.

Much of the *cholesterin*, if not all, is possibly merely excreted by the liver; it is most likely a nerve derivative, and in some conditions of nerve irritation it is said to be greatly increased (Flint). The *mucin* comes from the epithelium of the biliary passages and not from the hepatic cells.

Tests and Reactions.—*To obtain bile for analysis*, dilute some of the fresh secretion with water, and treat the mixture with spirit or dilute acetic acid; shake well and filter. The filtrate will serve for the general tests; but to obtain purified bile for analytical purposes mix the bile with 5 times its volume of absolute alcohol, filter after some time, and evaporate the filtrate to dryness. The residue dissolved in water gives the reactions well. The tests for bile depend on the identification of two of its constituents, the biliary acids and the pigments.

The presence of biliary acids is generally ascertained by the red or purple coloration given with sulphuric acid and sugar—Pettenkofer's *test*, which has been variously modified—while the pigments are generally detected by the play of colors given with an oxidizing reagent like nitric acid. The Pettenkofer's test as applied to urinary products is somewhat deceptive, as the urochrome, etc., yield red and purple colorations with sulphuric acid; but doubt can be set at rest by the use of the spectroscope, bile giving a broad dark band overlying D, two or three other bands occasionally being seen. A great many organic bodies besides the biliary acids give purple colorations with sulphuric acid alone, or with sulphuric acid and sugar; but such bodies are rarely met with in bile or biliary urine.

1. Pettenkofer's *Reaction for the Biliary Acids*—(*a*) Add to some bile in a test tube, or to a fluid containing it, a little sugar, then an equal volume of strong sulphuric acid, which is to be allowed to trickle down the side of the inclined tube: a strongly colored layer forms immediately above the level of the acid, which takes a purple tint on slight agitation. This purple layer gives two absorption bands, one near E and the other beside F, when examined spectroscopically (Schenk); but it has also been given as a band outside D and a broad band at E (MacMunn); and according to Heynsius and Campbell in the case of sodium taurocholate there are three bands, one between C and D, a second between D and E, and a third near F. These bands are not given by the purple-colored fluid obtained in the same way with albumens, etc.; further, the red fluid obtained in Pettenkofer's reaction is dichroic, while that got with albumen, etc., is not so.

(*b*) Dip a piece of filter paper in the diluted bile after having added to it a little cane sugar; dry the paper, and place a drop of sulphuric acid upon it: a violet red color will appear in a few seconds (Rosenbach and Strassburg).

(*c*) Place a little bile, and about two-thirds its volume of sulphuric acid, and one to two drops of a solution of cane sugar (10 per cent.) in a dish over a water bath; heat up to 70°, and a purple violet coloration will be obtained. The presence of nitrates or chlorates interferes with the reaction.

(*d*) I have employed the following modification of PETTENKOFER'S test for some years past, and have found it work delicately and satisfactorily. As it depends on the coloration of the froth obtained by shaking the fluid containing the bile, it is often advisable, so as to obtain as permanent a froth as possible, to mix the biliary fluid with a little mucilage of gum arabic before adding the syrup, though if much bile is present this is not necessary. The test tube must next be vigorously shaken for a short time, and when a deep layer of froth has formed a few drops of strong sulphuric acid are allowed to trickle down into it, when a beautiful violet or purple coloration will make its appearance, either at once or after the side of the tube has been very gently warmed.

2. GMELIN'S *Test for the Biliary Pigments.*—Nitric acid added to bile gives a precipitate which disappears on the addition of fresh acid, a play of colors being produced—green, blue, violet, red, and finally yellow. This test may be applied in various ways. A very good plan is to spread a drop of the diluted bile on a white porcelain dish, and then allow a drop of yellow nitric acid to flow into it, when the rings of color will appear at the point of contact.

3. *Absorption Spectrum of Bile.*—Hepatic bile is clear, but after having lain in the gall bladder it becomes darker colored, denser, ropy, and charged with much mucus. When fresh it gives an absorption band between D and E, but nearer D. After some time the bile alters, becoming dichroic and presenting four absorption bands.

Examine also a filtered dilute hydrochloric acid extract of dog's bile with the spectroscope, and a narrow band will be found between *b* and F.

Before applying any of these tests to fluids containing bile, it is often advantageous to separate the biliary acids and pigments, which is particularly necessary when the amount of bile present is very slight.

4. *Separation of some of the Biliary Constituents.*—Dilute some bile with water and add alcohol: a precipitate of mucus occurs: filter, and to a little of the filtrate add hydrochloric acid, when glycocholic acid will be thrown down in flakes; to the rest of the filtrate add acetate of lead solution: glycocholate of lead will be precipitated, and from the filtrate taurocholate will be obtained by the addition of subacetate of lead.

5. *To Analyze the Bile* (GORUP BESANEZ).—(*a*) Weigh 20 grams in a tared capsule, and, having evaporated to dryness, heat the residue for some time to 110°; weigh on cooling.

(*b*) Exhaust the dry mass with absolute alcohol, and collect the insoluble residue, which consists of *mucin*, a *little pigment*, and ***insoluble salts***; dry and weigh as before; then incinerate in a platinum capsule: the ***salts*** remain behind.

(*c*) The alcoholic extract is evaporated to a small volume, excess of ether added, and the mixture laid aside for several days; decant the ether carefully and wash repeatedly with fresh ether. The precipitate consists of the ***salts of the biliary acids***. Dissolve in a little alcohol, evaporate in a porcelain capsule, and having dried the residue weigh.

(*d*) The ethereal extract is to be distilled, the residue well dried over sulphuric acid *in vacuo*, and weighed; it consists of *cholesterin*, *fat*, and ***lecithin***. To separate the fat and lecithin from the cholesterin boil gently with caustic potash, which saponifies the fat and lecithin; shake well with a little water, and then with ether to dissolve up the cholesterin; the ethereal extract is to be evaporated, and the residue, when washed with a little water, dried at 100°, and weighed, gives the cholesterin.

6. *To Detect Bile in Vomited Matters.*—The bile, if present, generally imparts a green color and a bitter taste to the fluid; much mucus also is usually present. Shake up the vomit with water and filter through a linen cloth; precipitate the filtrate with plumbic acetate, and wash the precipitate on a filter; then digest it with sodic carbonate to remove the pigment, and evaporate to dryness; treat the residue with alcohol, filter, and evaporate the filtrate. The residue dissolved in a little water is then tested for biliary acids.

Pathology.—1. The *total amount* is probably diminished in the beginning of fevers. 2. The *solids are increased* especially in severe abdominal affections, in certain diseases of the heart where the hepatic circulation is embarrassed, in cholera, and in retention of bile; but they are *diminished* in pneumonia, tubercle, dropsy, and diabetes.

3. The *biliary acids and pigments* are much diminished in typhoid fever, and the bile in this disease, as well as in typhus, may become acid. The *pigments* may be wanting in fatty degeneration of the liver, and the *biliary acids* may disappear in some cases of amyloid degeneration. The *pigments* are increased, often more than doubled, in jaundice. Bile has a solvent action on the colored corpuscles of the blood, and it is possible that in cases of jaundice this solution may occur. 4. *Leucin*, *tyrosin*, and much *fat* may be present in typhus and typhoid fever. 5. *Crystallized fat* or *balls of fat* may be met with in tuberculosis. 6. *Sugar and glycogen* may appear in diabetes, as well as after injection of sugar into the veins; both are diminished in fever. 7. *Albumen* is occasionally present in fatty degeneration of the liver, in Bright's disease, and after the injection of much water into the veins. 8. *Urea* may appear in the bile in Bright's disease, cholera, etc.

In certain chronic affections the flow of bile is hindered, and it becomes concentrated, frequently leading to a deposit of cholesterin crystals, crystallized fat being frequently formed under similar circumstances. The same has also been noticed in chronic nephritis and hydrothorax.

The amount of bile, but chiefly its water, is increased by the ingestion of such bodies as calomel, podophyllin, aloes, rhubarb, scammony, taraxacum, and different laxatives (SCOTT, RUTHERFORD, RÖHRIG).

Bile acids, when injected, tend to destroy the blood corpuscles, as well as to produce parenchymatous degeneration of the glands and muscles; and, by acting on the cardiac ganglia, cause a slowing of the pulse (LEGG, STEINER); a spasm of the respiratory muscles is likewise said to be produced, and the urine becomes darker in tint.

Biliary calculi are rounded, ellipsoidal, or polyhedric, generally smooth, but sometimes covered with small mulberry-like projections, and either crystalline or amorphous in structure; they are of all sizes up to that of a nut, though occasionally much larger; their number also varies, as many as 7,000 having once been found in a gall bladder (OTTO). These calculi are formed by the deposition in the insoluble state of certain of the constituents of the bile around flocculi of mucus or epithelium. The most frequent are cholesterin, bilirubin, biliverdin, and carbonate of lime. The dark-colored calculi are richest in bilirubin, while the pale and often crystalline calculi are chiefly cholesterin. Most commonly these different bodies are present in varying proportions in the same calculus; thus in man they consist most frequently of cholesterin (generally over 95 per cent.) mixed with varying amounts of pigments and lime salts. Calculi of carbonate and phosphate of lime are the least frequent. Most biliary calculi contain traces of fat, biliary acids, mucus, and epithelium in addition to their chief components. Calculi of the ox usually contain very little cholesterin, about a half or a third of their mass consisting of bilirubin combined with lime.

CHAPTER XI.

THE BILIARY ACIDS.

The bile of most animals contains alkaline salts of taurocholic and glycocholic acids. Both bodies are characterized by the readiness with which they can be split up by their hydration under the influence of prolonged boiling with alkalies or mineral acids.

$$\underset{\text{glycocholic acid.}}{C_{26}H_{43}NO_6+H_2O} = \underset{\text{cholic or cholalic acid.}}{C_{24}H_{40}O_5} + \underset{\text{glycocin.}}{C_2H_5NO_2}$$

$$\underset{\text{taurocholic acid.}}{C_{26}H_{45}NSO_7+H_2O} = C_{24}H_{40}O_5 + \underset{\text{taurin.}}{C_2H_7NSO_3}$$

The prolonged action of these reagents may cause the cholic acid to be broken down still further and furnish a resinous product, *dyslysin* ($C_{24}H_{36}O_3$), insoluble in water and alcohol, but readily soluble in ether; indeed, cholic acid under the influence of heat alone, or of heat and hydrochloric acid, may be thus decomposed.

In human bile a body called anthropoglycocholic acid ($C_{18}H_{28}O_4$) has been described (H. Bayer).

Possibly much of the biliary acids secreted in the bile, particularly the glycocholic, is absorbed again and re-excreted, the absorption occurring chiefly in the jejunum and ileum, for Schiff found that the establishment of a biliary fistula in a dog quickly lowered the total amount formed, but that this was as quickly raised if the bile was re-injected into the small intestine. Tappeiner's experiments also prove the same thing.

In human bile glycocholic acid is much in excess of the taurocholic (Socoloff, Trifanowski, Jacobsen).

Preparation.—Different methods have been given, of which a few have been selected which the author has found effective.

1. Evaporate ox bile to a thick syrup, stirring it frequently with a glass rod, digest this with cold absolute alcohol, which leaves the pigments, part of

the mineral salts, and the mucus undissolved; then filter the alcoholic extract through animal charcoal, or shake it well and boil it with the charcoal, and filter. This alcoholic extract may also be made by rubbing up the bile with sufficient animal charcoal to form a paste, which is to be well dried over a water bath, reduced to a powder, and then extracted with absolute alcohol.

The alcoholic extract having been made, the alcohol is to be distilled off, the dry residue dissolved up in a little absolute alcohol, and the solution treated with ether until it becomes markedly turbid. A whitish mass is deposited in a few hours or days, which gradually assumes more or less of a crystalline appearance. This is PLATTNER's *crystallized bile*, and consists of a mixture of glycocholate and taurocholate of soda. By dissolving this in a small volume of water, adding a little ether and then dilute sulphuric acid, and stirring well, *glycocholic acid* crystallizes out in shining needles, the taurocholic acid remaining in solution; the crystals may be collected on a filter, washed with water, redissolved in very dilute spirit, and precipitated with excess of ether.

Or to a solution of PLATTNER's *crystals* add neutral and then a little basic lead acetate, when *glycocholate of lead* will be thrown down; collect on a filter, wash, dissolve in hot alcohol, and remove the lead by passing a current of sulphuretted hydrogen through it; filter, and by the careful addition of water to the alcoholic filtrate crystals will be deposited. To the previous filtrate from the glycocholate of lead add acetate of lead and ammonia, collect the *tauro-cholate of lead* precipitated, and wash and decompose it as with the glycocholate.

2. Evaporate ox bile nearly to dryness, extract with alcohol (90 per cent.), filter, distil off the alcohol from the filtrate, and treat the residue with water; to the watery solution add some milk of lime, warm gently, and filter. When the yellowish filtrate cools treat it with excess of dilute sulphuric acid until a permanent turbidity appears. Lay aside until a crystalline precipitate forms, which will occur sooner or later. Collect and wash it on the filter with cold water; it is then to be expressed, and dried between folds of blotting-paper, dissolved in excess of lime water, and again treated as before with dilute sulphuric acid. The *glycocholic acid* precipitated after some time (days, or even weeks) becomes crystalline.

3. The concentrated fresh ox bile is poured into high narrow glass cylinders, covered with ether, and then treated with a sufficiency of hydrochloric acid (2 c.c. acid to every 40 c.c. of fresh bile). The bile becomes crystalline. Pour off the ether, and shake the residue with much water; collect it on a filter, and wash it there with cold water until the washings are colorless; now dissolve the residue in hot water and filter. When the filtrate cools the *glycocholate* will crystallize out.

4. Evaporate dog's bile to a syrup, exhaust this with alcohol, and shake the alcoholic extract with animal charcoal to decolorize it; then evaporate to dryness, redissolve in a little warm absolute alcohol, filter again, and precipitate with excess of ether.

The pigment may be removed, as in method 1, by first making the bile into a paste with the charcoal, then evaporating to dryness and extracting the dry residue with a little absolute alcohol, to which excess of ether is to be added. The precipitate of *taurocholic acid*, which appears slowly, assumes a crystalline character; to purify it dissolve in a little water, precipitate the solution with basic lead acetate and ammonia, and wash the deposit with water; then digest it with boiling absolute alcohol and filter hot; pass a current of hydric sulphide through the filtrate and separate the lead sulphide by filtration; this last alcoholic filtrate is to be evaporated to a syrupy consistence at a low temperature, and the *taurocholic acid* thrown down by the addition of excess of ether.

Properties.—(*a*) The *glycocholic acid* exists in two forms, one of which crystallizes in very fine needles, and the other is amorphous, appearing as a resinous mass. It is monobasic, and enters into combination with the alkalies and alkaline earths, also with silver and lead. This acid is soluble without alteration in hydrochloric, sulphuric, and acetic acids and glycerin; easily soluble in alkaline solutions, with the formation of salts; very slightly soluble in cold, but more soluble in hot water; almost insoluble in ether, but very soluble in alcohol. Its alcoholic solution exerts right-handed polarization = 29°, the glycocholate of soda being = 25·7°.

This acid appears to be absent from the bile of carnivora, but it is abundant in ox bile and in human bile.

(*b*) *The taurocholic acid* (*choleic acid*, STRICKER), or at least its soda salt, forms silky needles that deliquesce readily in the air, forming an amorphous mass that soon passes into a syrup, being very unstable, and decomposing readily into taurin and cholalic acid. It is soluble in water and alcohol, and polarizes to the right, its soda salt in alcoholic solution having a specific polarizing power of 24·5°, but in watery solution only equal to 21·5°. It combines with potash, soda, and baryta, and its solutions are precipitated by basic acetate of lead and ammonia, but not by neutral acetate, like the glycocholate.

This acid is especially plentiful in the bile of the carnivora, being the only one present in dog's bile, but it is to be found also in ox and human bile.

Tests for the Biliary Acids.—1. To the solution of the biliary acids add a little solution of cane sugar, and then drop by drop strong sulphuric acid; a white cloudy appearance is produced, which disappears with excess of acid, a deep purple violet color being produced.

2. If present in small amount in liquid, evaporate this, and digest the residue with alcohol, and evaporate the alcoholic residue in turn. Add a few drops of water to the dry extract, and then a drop or two of syrup (1 to 3 water); let strong sulphuric acid now fall drop by drop into the mixture, and an orange color, rapidly passing through a carmine to a purple tint, shows itself, but soon disappears. The quantity of water must be small, and the temperature below 60°.

The reaction can often be satisfactorily obtained by adding a drop of sugar solution ($\frac{1}{5}$ per cent.) and a drop of sulphuric acid to the dry residue, and gently heating over a water bath until a violet red coloration begins to show itself at the margin of the liquid, when the capsule is to be removed and laid aside. The color increases in intensity.

The charring of the sugar (as in the case of diabetic urine) by the sulphuric acid sometimes hinders the characteristic reaction, particularly if the temperature rises too high; so DRECHSEL has proposed the use of a syrupy solution of phosphoric acid instead of sulphuric, the heat being applied as before.

In addition to the biliary acids, oleic acid, cholesterin, lecithin, benzin, phenol, turpentine, camphor, salicylic, tannic, and pyrogallic acids, morphia and various fats are said to give PETTENKOFER's reaction with sugar and sulphuric acid: and with sulphuric acid alone the reaction can be obtained with cod-liver oil, cerebrin, salicin, piperin, etc. The latter bodies appear, therefore, to contain a radicle related to sugar. The colored body produced appears to depend more on the constitution than on the composition of the product (KINGZETT).

By means of the spectroscopic test any difficulty with regard to the possible presence of albumens, fatty acids, amyl alcohol, etc., may be avoided, as a moderately strong solution of the biliary acids gives an absorption band between D and E, but nearer E, and a second beside F towards its red side (SCHENK).

3. The amount of biliary acids present in bile or in a liquid can be determined approximately by means of the polariscope with an alcoholic solution: $p = \frac{a \times 56{\cdot}4}{26{\cdot}4}$, a = deviation in degrees with a 1-decimetre tube.

4. *Quantitative Determination of Taurocholic Acid.*—By burning a weighed quantity of dry bile, which has been freed from every trace of sulphuric acid by baryta water, with nitric acid, the sulphur of the taurocholic acid is oxidized. Digest the residue with water and determine the sulphuric acid by baryta (see *Acidimetry*), 98 parts sulphuric acid = 32 sulphur, and 1 part sulphur = 16·8 taurocholic acid.

Derivatives.—j. **CHOLIC or CHOLALIC ACID,** $HC_{24}H_{39}O_5+H_2O$, is principally interesting as being the starting point of the biliary acids. It is the constant product of the decomposition of the biliary acids, and accordingly is found in the intestinal contents, and occasionally in the urine of jaundice, but it is not present in fresh bile nor in the organism.

It is readily obtained by the action of acids or boiling alkalies on the biliary acids, but BAYER affirms that the cholic acid derived from the human biliary acids is quite different to that prepared from ox bile by STRICKER'S method, and HAMMARSTEN agrees with him in this respect in some points.

It is **prepared** by boiling bile with caustic potash for 12 to 24 hours; then precipitate with hydrochloric acid, and having washed the deposit with water dissolve it in caustic soda containing a little ether; hydrochloric acid is next added, and after some time crystals form; decant and cover the residue with ether, drain off the ether in half an hour or so, and dissolve the deposit in boiling alcohol; to this solution add a little water until a permanent precipitate appears; tetrahedric crystals soon make their appearance.

Properties.—It is almost insoluble in water, soluble with difficulty in ether, and moderately soluble in alcohol. Cholic acid occurs in an amorphous as well as in three crystalline forms; it is monobasic, and by prolonged boiling with acids and alkalies, as well as by putrid decomposition, it is transformed into choloidic acid ($C_{24}H_{38}O_4$) and later into dyslysin ($C_{24}H_{36}O_3$). If nitric acid is employed, and the boiling continued for five or six days, a good condenser being attached to the vessels, acetic and other volatile fatty acids are evolved, and cholesteric ($C_8H_{10}O_5$) and choloidanic acids ($C_{16}H_{24}O_7$) remain behind in the retort.

ij. For **GLYCOCIN,** one of the decomposition products of glycocholic acid, see under Hippuric Acid, Book IV, Chapter X.

iij. **TAURIN,** $C_2H_7NSO_3$.—This body is found in the intestinal canal, kidneys, spleen, lungs, and in putrid but not fresh bile, being developed at the expense of the taurocholic acid when the bile ferments.

It is isomeric with isethionamid, and ammonium isethionate when heated to 210° to 220° is converted into amidethyl sulphonic acid, or taurin—

$$C_2H_4\begin{cases}OH\\SO_3NH_4\end{cases}=H_2O+C_2H_4\begin{cases}NH_2\\SO_3H\end{cases}.$$

Preparation.—Concentrate fresh ox or dog's bile and boil it several hours with dilute hydrochloric acid, adding water from time to time to replace the loss by evaporation; dyslysin separates, and afterwards some sodic chloride; decant and filter, evaporate the filtrate to dryness, and digest the residue with absolute alcohol, which precipitates the taurin and removes the glycocin chlorhydrate. The residue, insoluble in the alcohol, is dissolved in water and left to crystallize, when more sodic chloride separates, the taurin remaining in solution. To the decanted liquid add 4 to 5 times its volume of boiling alcohol, which takes up the taurin, this body afterwards separating in prismatic crystals when the alcohol cools. To purify it the taurin may be repeatedly dissolved up in water, and crystallized out by the addition of alcohol.

Properties.—Taurin crystallizes in large four or six-sided colorless prisms soluble in hot water and insoluble in alcohol: it is not decomposed by boiling dilute acids or alkalies, but nitrous acid breaks it up into isethionic acid, water, and nitrogen. Combinations with soda, lime, silver, lead, and mercury, etc., are known as—

$$C_2H_6(Na)NSO_3,\ (C_2H_6NSO_3)_2Ca,\ (C_2H_6NSO_3)_2Hg+HgO.$$

CHAPTER XII.

THE BILIARY PIGMENTS.

THE two normal pigments are *bilirubin* and *biliverdin*, but the freshly secreted bile poured out during digestion which has not lain in the gall bladder appears to contain bilirubin alone. Two others are described by STÄDELER, *bilifuscin* and *biliprasin* which are met with chiefly in biliary calculi; *bilihumin* has also been described, and HAMMARSTEN further gives *hydrobilirubin*. These pigments play the *rôle* of weak acids. According to STÄDELER the following relationship exists among some of these coloring principles: biliverdin is bilirubin $+O$ and H_2O; biliprasin the same, only with an additional molecule of water; and bilifuscin, bilirubin $+2H_2O$.

Bilifuscin ($C_{16}H_{20}N_2O_4$) is found in small quantity in old bile obtained from the *post-mortem* room, and in human gall stones; *biliprasin* ($C_{16}H_{22}N_2O_6$), in human gall stones in small amount; while *bilihumin* is an impure product.

Bilirubin, of which the rest seem to be derivatives, is closely related to hæmatin, a derivative of hæmoglobin—

$$3(\underset{\text{(hæmatin.)}}{C_{32}H_{36}N_4FeO_6})+3H_2O=6(\underset{\text{(bilirubin.)}}{C_{16}H_{18}N_2O_3})+3FeO.$$

BILIRUBIN (**Bilphæin, Bilifulvin, Cholepyrrhin**), $C_{16}H_{18}N_2O_3$ or $C_9H_9NO_2$ (THUDICHUM).—This pigment is present in the free state in the bile of man and carnivora, but more abundant in ox bile; also in large amount in gall stones, particularly those of a dark color, in which it is partly combined with some of the alkaline earths, etc. It constitutes the chief biliary pigment, and is probably more or less identical with hæmatoidin, the blood crystals found in old extravasations (VALENTINER).

Preparation.—1. Powder richly colored *biliary calculi*, *particularly those of the ox*, and exhaust the powder with ether, and subsequently with boiling water, to which a few drops of hydrochloric acid should be added to separate the bilirubin from its combinations. Wash it now in pure water and dry it. The residue is next boiled with chloroform and filtered; from the filtrate the chloroform is distilled off, and the residue extracted with absolute alcohol and ether, by which bilifuscin is removed, the bilirubin remaining behind. It may now, to purify it, be redissolved in chloroform, and the solution allowed to evaporate spontaneously for some time, and then the bilirubin thrown down as an amorphous orange precipitate by the addition of alcohol (after STÄDELER). Some of the bilirubin may be obtained in the crystalline form by allowing part of the chloroform solution to evaporate to dryness.

The residue after the chloroform extraction contains generally a green coloring matter, *biliprasin*, which can be removed by means of alcohol, the alcoholic extract evaporated, the residue purified with ether and chloroform, and then dissolved up again in a little cold alcohol.

After the action of all these solvents upon gall stones a brown body, *bilihumin*, usually remains behind.

2. *From Human Bile.*—Add an excess of alcohol, and then a little ammonia and calcic chloride, filter, and exhaust the precipitate with alcohol. The residue is treated with dilute hydrochloric acid, and after having been washed with water is extracted with alcohol, which dissolves out the bilifuscin, while the insoluble part is digested with chloroform, which dissolves up the bilirubin (THUDICHUM).

Or dilute the bile with water, precipitate with milk of lime, then pass a current of carbonic acid for some time to separate the lime, and filter; decompose the precipitate with a little hydrochloric acid, then shake it up with chloroform, and after having evaporated off much of the chloroform precipitate the bilirubin with alcohol.

3. It can readily be extracted from fresh dog's bile by acidifying this with acetic acid, adding chloroform, then warming gently and shaking well in a flask. Allow the chloroform extract to settle, and remove it with a pipette. The bilirubin can be separated from the chloroform by evaporation or precipitation with alcohol.

Properties.—It forms a fine orange or red amorphous, or a dark brownish red, crystalline powder, the crystals forming rhombic tables or prisms, soluble in the alkaline carbonates and precipitable therefrom by hydrochloric acid; readily soluble also in chloroform and benzole, although its alkaline combinations are insoluble in these reagents; but very sparingly soluble in alcohol and ether. Its color is evident even in very dilute solutions. Bilirubin acts the part of a weak acid, and combines with soda, lime, silver, baryta, lead, etc., as $(C_{16}H_{17}N_2O_3)_2Ca$.

Derivatives and Characteristics.—1. Add some moderately strong yellow nitric acid, drop by drop, to an ammoniacal solution of bilirubin; a green coloration appears, which rapidly changes to a blue (*bilicyanin*), a violet, a red, and then an orange and yellow tint.

Zones of color will also be obtained by placing drops of the bilirubin solution and of yellow nitric acid in contact upon a white plate.

The final product of the reaction is called *choletelin* ($C_{16}H_{18}N_2O_6$) by MALY. It is a yellowish brown amorphous body, soluble in water, acids, and alkalies, and it is stated by MALY to be identical with the urinary pigment. Into hydrobilirubin it is convertible by the action of water and sodium amalgam, and this in turn reconvertible into choletelin by nitric acid.

Choletelin gives one broad band extending from *b* to a little beyond F. Jaffé's urobilin also gives a band at F. While choletelin is the final oxidation product, urobilin appears to hold somewhat of an intermediate position. Another secondary product of the oxidation of bile pigment is described by Stokvis as insoluble in ether and chloroform, but forming a rose-red solution in caustic soda, which gives a broad band in the green between D and E; but this pigment is not found in urine unless in pathological conditions.

2. Add to a solution of the bile pigments in alcohol, ether, or chloroform an alcoholic solution of bromine (5 per cent.) or an aqueous solution of chloric or iodic acids (20 per cent.), and three stages of coloration will be produced—green, blue, and violet—after which a reddish yellow color shows itself, and lastly the whole becomes colorless.

The blue solution gives one band in the red when examined with the spectroscope; the violet solution two bands, one in the red and the other in the indigo; and the reddish yellow solution a single band in the blue (Capranica).

3. Add a little sodium amalgam to an alkaline solution of bilirubin, and heat gently or lay aside for two or three days; the color will gradually disappear. The mercury is then separated by decantation, and hydrochloric or acetic acid added until a precipitate occurs in the form of reddish brown flocculi, that are to be separated by filtration. This body is *hydrobilirubin* ($C_{32}H_{44}N_4O_7$), said to be identical with Jaffé's *urobilin* (Stokvis) and with the coloring matter, *stercobilin*, of the fæces (Masius). According to Hoppe Seyler a similar body can be prepared by acting on hæmoglobin or hæmatin with hydrochloric acid and tin.

HYDROBILIRUBIN (**Stercobilin**) is dark brown and amorphous, and soluble in alkalies, sulphuric and acetic acids, and alcohol, ether, and chloroform. The solutions are generally rosy red in thin layers; but they do not show a play of colors with nitric acid. Its acid solutions are said to give an absorption band, especially on the addition of a little chloride of zinc, between *b* and F, but close to the latter.

Hydrobilirubin is occasionally present in bile and urine, but is usually present in fæces, being formed there probably by the action upon the bilirubin of the nascent hydrogen evolved in butyric acid fermentations.

BILIVERDIN, $C_{16}H_{18}N_2O_4$ (Maly), $C_{16}H_{20}N_2O_5$ (Städeler), $C_8H_9NO_2$ (Thudichum).—This body is abundant in the bile of cold-blooded animals, as well as in that of warm-blooded animals who are starving.

An alkaline solution of bilirubin, when exposed to the air, becomes greenish from the formation of biliverdin. The action of light alone has been said to be sufficient to induce the change (Capranica).

Biliverdin is prepared by making an alkaline solution of bilirubin, passing a current of air through it or exposing it to the air for some time in a flat vessel until it becomes intensely green; then precipitate with hydrochloric acid, wash the deposit with water until no chlorine reaction can be obtained in the washings; finally dissolve in absolute alcohol and precipitate with water.

Properties.—Biliverdin forms a green amorphous powder, and is insoluble in water, ether, and chloroform; it is very soluble in alcohol (particularly if freshly prepared), acetic acid, and alkaline fluids. Like bilirubin it gives a play of colors with nitric acid, and from it hydrobilirubin and choletelin can be obtained.

Relations among the Soluble Pigments of the Body.—It is supposed that the bile pigments are derived from those of the blood, and give origin to the pigments of the fæces, from which come the coloring matters of the urine. The order of their appearance would, therefore, be somewhat as follows: hæmoglobin, hæmatin or hæmatoidin, bilirubin, hydrobilirubin, and urochrome. As yet, however, the connection has not been clearly proved.

CHAPTER XIII.

CHOLESTERIN.

CHOLESTERIN, $C_{26}H_{44}O$, is very widely spread in the body, and in the seeds of plants it has also been found. It occurs largely in the cerebro-spinal axis and in nerves; is also present in blood and is possibly excreted in the bile, forming the chief ingredient of biliary calculi. Its natural solvents in the bile are the soaps and biliary acids. Cholesterin is likewise found in yolk of egg, in the spleen, in certain dropsical fluids, pus, atheromatous deposits and strumous cysts, and in many lipomas, goitres, and pulmonary tubercular deposits.

Preparation.—1. Powder some pale biliary calculi, boil the powder some hours with spirit to which potassic hydrate has been added; filter on cooling, and wash the crystalline mass with cold alcohol and then with water; purify the cholesterin thus obtained by redissolving it in boiling ether, adding to this last half its volume of alcohol, and lay aside to evaporate spontaneously.

2. It can also be readily obtained by extracting brain substance. The pieces of brain are to be placed in alcohol for several days, and then to be finely divided and digested in boiling alcohol; the hot extract is next filtered through a heated funnel, and the filtrate allowed to cool. The deposit that occurs consists of cerebrin and protagon as well as cholesterin. This is first washed with cold alcohol, and after being dried with filtering paper is shaken with ether, the ether distilled off, and the residue heated for an hour with an alcoholic solution of potassic hydrate; it is then evaporated to dryness, washed with water, and dissolved in a mixture of ether and alcohol, from which the cholesterin is allowed to crystallize out.

Properties.—Cholesterin has the character of a monatomic alcohol, seeming to be the only free alcohol that occurs in the body. It is a fatty substance insoluble in cold water, alkalies, dilute acids, and alcohol, but soluble in a large quantity of boiling water or in boiling acetic acid, glycerin, or alcohol; also readily so in ether and chloroform, benzole, soaps, and the biliary soda salts.

It exists water-free or combined with a molecule of water. Out of benzole, chloroform, or anhydrous ether it crystallizes without water, but water holding crystals are deposited from alcohol in the form of oblique rhombic tables. From a mixture of alcohol and ether it separates in monoclinic prisms or large pearly plates. The usual crystals are the large, thin, translucent, and mother-of-pearl-like rhombic tables. The anhydrous silky needles are not so common.

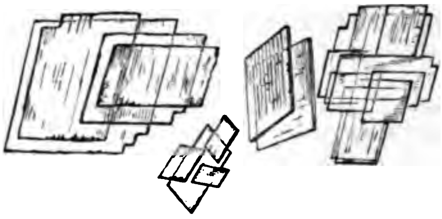


FIG. 17.—CRYSTALS OF CHOLESTERIN.

Heated up to 350° *in vacuo* it sublimes in great part without alteration, and yields cholesteric acid ($C_8H_{10}O_5$) when boiled with nitric acid; when heated to 200° with such acids as acetic and benzoic it forms compound ethers, and a resinous hydrocarbon ($C_{26}H_{42}$) appears when it is boiled with strong sulphuric acid.

Tests and Characteristics.—1. Add a little dilute sulphuric acid to a few crystals, warm gently, and then add a drop of strong sulphuric acid: a deep red color is developed. This test can be well applied to a few crystals placed on a slide and examined under the microscope. Add to the crystals a drop or two of strong sulphuric acid diluted with one-fifth its volume of water; after mixing with a glass rod heat the slide gently. The edges of the crystals will be seen under the microscope to have become violet or carmine-tinted (MOLESCHOTT).

2. When the crystals are heated with moderately strong sulphuric acid and afterwards with a little iodine, a play of colors is produced, passing from violet through blue, green, red, and yellow to brown. Concentrated sulphuric acid colors the crystals red, the tint being changed to green on the addition of water.

3. Dissolve some crystals in chloroform, and shake the solution with an equal volume of strong sulphuric acid: a blood red solution is obtained, which becomes blue, then green, and finally yellow. A trace of water decolorizes the solution at once (SCHIFF). The layer of sulphuric acid presents a well-marked green fluorescence; on diluting it with glacial acetic acid a rosy and then a purple liquid makes its appearance, but the flourescence remains permanent (SALKOWSKI).

4. Heat some crystals gently with a mixture of ferric chloride (1) and hydrochloric acid (2), and they will, if pure, assume a violet or bluish color.

5. Place a few crystals on a small porcelain dish, cover them with a drop of strong nitric acid, and evaporate to dryness at a gentle heat; on touching the yellow residue before it has quite cooled with a drop of ammonia a deep red color is produced, which is not altered by the addition of a drop of caustic potash—thus differing from murexid (SCHIFF).

BOOK III.

THE TISSUES: CHEMISTRY OF THE TISSUES, ORGANS, AND REMAINING SECRETIONS.

CHAPTER I.

THE BLOOD.

Functions.—1. Serves as the great *medium of exchange* among all the parts of the body.

2. *Acts as the great carrier of nutrient fluid to the tissues.* The blood is elaborated from the food, and serves as the intermediary between it and the fluid in which the tissues and organs are bathed, and from which they obtain their nutriment. Waste is constantly going on, and this waste material is as constantly, during life, being replaced by new material supplied by the blood.

3. *It is also the great oxygen-carrier.* In the lungs the hæmoglobin fixes a certain amount of this gas, and conveys it to the interstitial fluids. By means of the oxygen thus conveyed oxidations are carried on in the tissues, by which the latent energies there present are converted into heat and the vital forces.

4. It further serves, like a drainage system, *to carry away the waste products*, such as carbonic acid and the like, to those parts of the economy, as the lungs, kidneys, etc., where they can be eliminated or prepared for elimination.

Physical Characters.—Blood is an opaque, viscid, red fluid, slightly alkaline in reaction, saltish in taste, possessing a mean density of 1055 and a temperature between 36·5° and 37·8° (97·7° to 100° F.)

(*a*) Its *color* is due to the hæmoglobin that it contains, and to the condition in which this body exists, whether chiefly in the state of oxyhæmoglobin or of reduced hæmoglobin, the degree of color also depending more or less on the proportion between its colored and pale corpuscles, and on the greater or less concavity of the former. Arterial blood is of a bright scarlet; venous blood of a dark bluish red color; arterial blood is also monochroic, while venous blood is dichroic—that is, red with reflected and bottle green with transmitted light. The color of arterial blood is darker in advanced pregnancy and paler in chlorosis, leukæmia, and diseases of the spleen. Venous blood from the kidney is lighter in color than other venous blood, and the same may be said of venous blood from an inflamed organ.

(*b*) The *odor* of fresh blood somewhat resembles that of butyric acid, and it is readily evolved by treating the blood with sulphuric acid, being probably due to some volatile body of the fatty acid series.

(*c*) The *density* may vary between 1045 and 1075 (or 1050 to 1059, NASSE and SCHMIDT), or an average of 1055, being somewhat less in women and children. The *corpuscles* have a density of 1088 to 1105; the *plasma*, of 1027 to 1028; and the *serum*, of 1026 to 1029, or an average of 1028.

(*d*) The *temperature* is due to the oxidation going on in the tissues. The temperature of the blood of the hepatic and portal veins is higher than that of ordinary venous blood, and the blood of the right ventricle is warmer than that of the left.

(*e*) The *alkaline reaction* is due to the bicarbonate of soda and sodic phosphate of the plasma. The alkalinity increases in the serum after coagulation, but the fresh blood is more alkaline immediately after removal than after a short time has elapsed (ZUNTZ). *To show this alkaline reaction* (1) treat some glazed violet litmus paper with strong sodium chloride solution, then touch it with a drop of blood to which a fresh drop of the sodium chloride has been added, and in a few seconds wipe away the whole by means of filter paper; the litmus paper will be seen to be colored blue by the blood (ZUNTZ). (2) Let a drop of blood fall on a thin slab of plaster of Paris which has been previously treated with neutral litmus solution. On washing the drop away a blue stain remains behind (LIEBREICH).

MALY' regards the ordinary method of titration of serum as not trustworthy, and his experiments would tend to show that the serum has acid instead of alkaline properties. HINTEREGGER has shown that acids and acid salts diffuse more readily than neutral salts; therefore serum containing acids ought to yield an acid diffusate. This MALY has found to be the case: 350 c.c. of serum dialysed in distilled water yielded a diffusate containing sufficient acid to neutralize 212 milligrams of soda.

Quantity of the Blood.—Very different estimates have been given, but the most reliable appear to be founded on the data of WELCKER and HEIDENHAIN, etc.; according to these the blood forms 7·7 to 8·3 per cent. of the body weight of an adult man; that is, for a man about ten stone weight, about eleven pounds of blood. This corresponds very closely to BISCHOFF'S estimate of one-thirteenth of the body weight. A new-born child contains in its body only a proportion of 5·2 per cent., or about one-nineteenth of the body weight; a dog about 7·4 per cent., and a rabbit 5·5 per cent.

Distribution.—It may be stated in general terms that about one-fourth of the blood is normally present in the liver during life; one-fourth in the muscles of the skeleton; one-fourth in the heart, lungs, and great vessels, and the remaining fourth in the rest of the organs and tissues.

Microscopic Constituents of the Blood.—These consist of a series o little bodies called *corpuscles*, which float in the *liquor sanguinis*. Of the corpuscles there are two chief varieties, the *colored* or *red*, and the *pale* or *white*

(*a*) The *colored corpuscles* vary in shape and size throughout the vertebrata; they are circular hollow discs in all the mammalia except the camelida in which they are oval, and they are oval in shape in birds, reptiles, and fish. In man they have an average diameter of $\frac{1}{3400}$ to $\frac{1}{3200}$ of an inch. In all the vertebrates except the mammalia the corpuscles are nucleated, but it should be mentioned that a body resembling a nucleus is said to be brought into view, even in a mammal's red corpuscle, by special treatment (BÖTTCHER). These colored corpuscles consist of a pale, translucent, white protoplasmic substance, the *stroma*, which is everywhere permeated by the red coloring substance of the blood, the hæmoglobin. No separable cell-wall is present, although something of the kind has been described in the red corpuscles of reptiles, and even of mammalia (RANVIER, RUTHERFORD).

Some small granular colored corpuscles have also been mentioned as existing in the blood; to these HAYEM has given the name of *hæmatoblasts*.

(*b*) Of the *pale corpuscles* there are different varieties. They are nucleated masses of protoplasm devoid of cell membranes and containing fine or coarse granules; they possess the power of amœboid movement, and can take substances into their interior. Intermediate forms also exist; and RANVIER describes two forms of free granulations, the one rounded and the other angular.

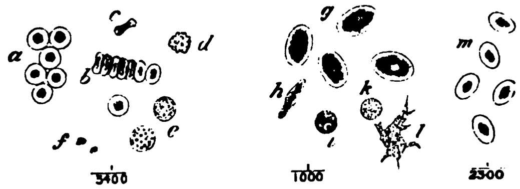


FIG 18.—BLOOD CORPUSCLES.
(*a* to *f* human, *g* to *l* frog, and *m* pigeon.)

a, red or colored human corpuscles seen on the flat; *b*, a rouleau of human corpuscles seen on the flat; *c*, a red corpuscle seen in profile; *d*, a crenated red corpuscle; *e*, pale corpuscles, one of which is coarsely and the other finely granular; *f*, free granulations; *g*, red corpuscles of frog; *h*, red corpuscles of frog seen in profile; *i*, dead pale corpuscle; *k*, resting pale corpuscle; *l*, pale corpuscle in a state of activity, exhibiting amœboid movement; *m*, red corpuscles of pigeon.

As a mean there is about one pale corpuscle to 340 red; but the pale corpuscles are increased by food, and the proportion varies according to the region whence the blood is derived: thus in the splenic vein there is 1 to 60 red, in the hepatic vein 1 to 170, in the portal vein 1 to 740, and in the aorta 1 to 2260.

Chemical Composition.—Normal blood left to itself for twenty-four hours gives the following percentages:—

Blood {
Liquor sanguinis { serum · 44–52·5
fibrin }
Corpuscles } clot · 47·5–56 { **moist corpuscles** = 35–36
interstitial serum = 12·5–20

The chemical composition varies somewhat in different animals, and even in the same animal there are sensible differences not only according to the region whence the blood is taken, but also according to the physiological or pathological condition of the animal at the time.

Analysis—Blood of Adult Male (æt. 25). (C. SCHMIDT.)

	Per cent.		Per cent.
Plasma	48·69	water	43·90
		solids	4·79
Moist corpuscles	51·3	water	34·97
		solids	16·34

	Corpuscles Per cent.		Plasma. Per cent.
Water	68·16		90·15
Solids	31·84		9·85
Globulin, etc.	29·60	Albumens Albuminates Extractives	8·19
Hæmatin	1·50		
(or Hæmoglobin 31·11)		Fibrin	0·81
Ash	0·73		0·85
Potassic Chloride	0·367		0·036
Sodic "	—		0·55
Potassic phosphate	0·234		—
Sodic "	0·063		0·027
Soda	0·013		0·15
Potassic sulphate	0·013		0·028
Calcic and magnesic phosphate	0·015		0·053

The amount of corpuscles in this analysis appears very high; in [illegible] in another analysis of the blood of a woman, aged 30, Schmidt obtained [illegible]d the proportions:—

Plasma	60·38
Moist corpuscles	39·62

Other chemists have given the mean of the [illegible]e plasma to the corpuscles as: plasma, 65–6[illegible]7 per cent.; corpuscles, 33–35 per cent.

The ash of the serum as compared with that of the corpuscles is [illegible]s rich in soda salts and chlorine, but poor in phosphates and sulphates. [illegible]s. It is possible, it may be remarked, that in the process of calcination [illegible]n the sulphuric and phosphoric acids are increased at the expense of the [illegible]e carbonic acid that is expelled, the chlorine at the same time diminish[illegible]ing sensibly. Analyses, at any rate, make the proportion of phosphoric [illegible]c acid in the corpuscles to that in the plasma as = 0·113 per cent. to [illegible]o 0·019 per cent.; and of the potash in the corpuscles to that in the [illegible]e plasma as = 0·332 per cent. to 0·032 per cent. On the other hand, [illegible], in the plasma the proportion of soda and chlorine is about three time[illegible]s as great as in the corpuscles; and there is also in the plasma an exces[illegible]s of the earthy phosphates.

Subjoined is the *mean composition of the blood* as given by BEC[illegible]QUEREL and RODIER:—

	Per cent.
Water	78·16
Dry corpuscles	13·50
Albuminoids	7·00
Fibrin	0·25
Fats	0·17
Extractives	0·84
Earthy phosphates	0·03
Iron	0·05

The *ash* of human blood is thus given by JARISCH in the 100 parts:—

Chlorine	30·74
Potash	27·55
Soda	24·11
Phosphoric acid	8·82
Sulphuric "	7·11
Oxide of iron	8·16
Lime and magnesia	1·33

1. As to *water*, the blood of the hepatic vein contains less than that of t[illegible]e portal vein. Fasting from solids and liquids causes the quantity to dim[illegible]ish; abstinence from solids alone increases it at first, but then causes it to si[illegible]k.

2. ***Fats*** are present in an average proportion of 0·2 per cent., and consist of palmitin, stearin, olein, and phosphorized fats analogous to those in the brain. They are especially abundant after food, and may thus rise to 0·4 to 0·6 per cent., and are richer in portal than in hepatic blood, and also in the blood of females than of males. Alkali soaps of the above fats are also found in the blood.

3. ***Extractives.***—Under this head are included all the organic constituents with the exception of the albumens and fats.

Cholesterin exists in the corpuscles as well as in the serum; it varies from 0·02 to 0·03 per cent., and is said to increase in old age.

Lecithin is probably a derivative of the destroyed corpuscles.

Kreatin = 0·108 to 0·055 per cent. in the blood of the ox. *Urea* forms 0·02 per cent. of the total blood (0·0192 per cent. in blood of dog—WURTZ); it is richer in placental blood.

A *ptyalin-like ferment* has been separated; also a *saccharine body* of the nature of *grape sugar*, forming about 0·05 per cent. of the total blood (0·04 to 0·07 per cent.—PAVY, DUPRÉ), but disappearing very rapidly after death unless the corpse is maintained at a temperature below 0°. While the portal blood contains little or no sugar, that of the hepatic vein contains from ½ to 1 per cent. of sugar in the dry residue. There is much difference of opinion as to the amount of sugar; being, according to some, most abundant in the hepatic vein, and then gradually disappearing, but more in arterial than in venous blood (BERNARD); while, according to others, there is no constant difference in the amount of sugar in arterial and venous blood (PAVY, ABELES).

	Carotid. Per cent.	Jugular vein. Per cent.	Right ventricle. Per cent.
According to BERNARD . . .	0·11 to 0·15	0·06 to 0·12	—
" MERING	0·17 " 0·13	0·14 " 0·15	—
" ABELES	0·049	—	0·054

Lactic acid, *xanthin*, *hypoxanthin*, *alcohol*, and *indican* are all described as present; also a *yellow pigment*, probably an oxidation product of hæmoglobin, or hydrobilirubin according to MALY.

4. *Inorganic Salts.*—A mean of 0·9 per cent. to the 21 per cent. of solids; more abundant in hepatic venous blood than in portal blood, and richer in the latter than in the serum of the blood of the jugular. Sodic chloride forms about ½ per cent. of normal serum; sodic carbonate and sulphate are also present in small proportion; the sodic phosphate probably exists as Na_2HPO_4, and the traces of magnesic and calcic phosphates as Mg_32PO_4 and Ca_32PO_4 (?) respectively.

The arrangement of bases and acids given in blood analyses, it should be remembered, is artificial and approximative, and cannot be said to be really a correct representation of the condition in which these bodies are present in the blood. Both phosphates and sulphates, for example, are no doubt derived in great part from the oxidation of the lecithin and proteids, etc.; the iron from the hæmoglobin; and the earthy phosphates in part from the fibrin and albumen, being set free by these bodies when they coagulate.

The Corpuscles.—These bodies constitute from one-third to a little less than one-half the whole blood. The blood of birds is richest in corpuscles, but not so rich in hæmoglobin as the corpuscles of human blood, which is richer in corpuscles than the blood of any other mammal. The red corpuscles, as we have seen, are made up of a colorless stroma, consisting of globin or a globulin-like body or bodies, which must not be confounded with the paraglobulin of the serum, although the latter may be derived from it. This globin is impregnated with hæmoglobin, and contains in addition traces of other bodies. The moist corpuscles of human blood contain about 35 per cent. dry solids. The dried organic matter, according to JÜDELL, consists in the 100 parts of—

Hæmoglobin	86·79 to 94·30
Albuminous bodies and nuclein	5·10 " 12·24
Lecithin	0·35 " 0·72
Cholesterin	— 0·25

There are also present alkaline chlorides and phosphates, a little fat, and traces of manganese and of a diastatic ferment. Nucleated corpuscles are said to be richer in albumen, cholesterin, and lecithin; and in their nuclei a body named nuclein (PLOSZ) has been described as present. This nuclein resembles mucin, but differs from it in containing phosphorus. The average of iron in the blood is said to be 0·054 per cent. (PELOUZE), and in the dry corpuscles 0·43 per cent. (BOUSSINGAULT).

The composition of the pale corpuscles can only be arrived at indirectly. They consist of several albuminous bodies, fat, lecithin, glycogen, and other extractives, together with potash phosphates, etc.

The Plasma, at a temperature below 0°, is a viscid, greenish yellow or yellowish fluid, strongly alkaline in reaction, and separating into fibrin and serum if the temperature is only a little raised above 0°. The generators of this fibrin, according to SCHMIDT, are fibrinoplastin (paraglobulin), fibrinogen, and a special ferment. Of these only the fibrinogen is said to be preformed, the fibrinoplastin and the ferment resulting from the rapid destruction of the pale corpuscles. In men the amount of fibrin that can be separated forms a mean of about 0·2 per cent. of the total blood; but arterial yields more than venous, and the blood of the jugular vein more than that of the portal. Its quantity is increased by animal to a greater extent than by vegetable food; it also increases in pregnancy.

The Serum is a transparent yellowish or greenish yellow fluid, alkaline, slightly viscid, and consisting of water about 90 per cent., holding in solution 8 to 10 per cent. of proteids and 1 to 2 per cent. of fats, extractives, and salts. Arterial serum contains more water than venous serum, and the water increases in old age (SIMON).

Three albumens are described as present—*serum albumen* (serine), *paraglobulin* (fibrinoplastin), and *alkali albuminate* (serum casein). HAMMARSTEN gives the total albumen as equal to 7·62 per cent., of which serum albumen forms 4·51 and serum globulin 3·10, the globulin therefore bearing the proportion to the serine of 1 : 1·51. WEYL considers that there is only one globulin in serum, *serum globulin*, fibrin and fibrinoplastin being merely this body mixed with some fibrin ferment.

The *ser-albumen* is soluble in water, and is precipitated by boiling, coagulating at about 71° in the presence of a little acetic acid.

The *paraglobulin* possibly comes from the colored corpuscles (KÜHNE) and is precipitated by a current of carbonic acid gas passed through the serum diluted with ten times its volume of water.

The *alkali albumen* is thrown down by the addition of acetic acid to the filtrate after the separation of the paraglobulin.

Traces of peptones are also occasionally met with.

The Gases of the Blood.—In the following table is given the average of a series of experiments (SCHÖFFER, PREYER, PFLÜGER, SCZELKOW, etc.) with the blood of dogs and sheep, the results being calculated in percentages at 0° and 760 mm.

I. *Arterial Blood.*

Total volume of gas disengaged *in vacuo* = 49 per cent.
Nitrogen . . . . = 2·47
Oxygen . . . . 15·65
Free carbonic acid = 30·88
Carbonic acid disengaged by the *action of acids in vacuo* . . . = 3·12
(Free carbonic acid and carbonic acid disengaged) = 34·00
Making a total . . . . . . = 55·12 per cent.

II. *Venous Blood.*

Total volume of gas disengaged *in vacuo* = 50·74 per cent.
Nitrogen . . . . = 1·38
Oxygen . . . . 9·36
Free carbonic acid = 40·00
Carbonic acid disengaged by the *action of acids in vacuo* . . . — 6·15
(Free carbonic acid and carbonic acid disengaged) = 46·15
Making a total . . . . . 56·89 per cent.

The average in human blood at 0° and 760 mm. may be thus stated (FOSTER):—

	Oxygen.	Carbonic acid.	Nitrogen.
Arterial blood . .	20 per cent.	39 per cent.	1 to 2 per cent.
Venous " . .	8 to 12 "	46 "	1 " 2 "

Or at 0° and 1,000 mm. (according to the German method)—

	Oxygen.	Carbonic acid.
Arterial blood	16 per cent.	30 per cent.
Venous "	6 to 10 "	35 "

Thus arterial blood contains on an average about 7 per cent. more oxygen and 6 per cent. less carbonic acid gas then venous blood.

The *amount of oxygen* varies according to the number of colored corpuscles—that is, to the quantity of hæmoglobin—in the blood, and depends greatly on the region of the body from which it is taken: for example, in the carotid artery the oxygen is present in the proportion of 21 per cent.; in the renal artery, 19 per cent.; in the renal vein, when the kidney is active, 17 per cent., and when in a state of rest, 6 per cent.; in the splenic artery, 14 per cent.; in the splenic vein, when the spleen is active, 11 per cent., and when at rest, 4 per cent.; the blood of the femoral artery also, when compared with that of the carotid, contains much less oxygen. Further, the state of the health and the character of the food appear to affect the amount and character of the gas considerably.

The *oxygen is combined with the hæmoglobin*, with the exception of a slight trace that is in a state of solution; accordingly corpuscle-holding serum absorbs 5 times as much oxygen as ordinary serum. 100 grams of hæmoglobin crystals dried between folds of blotting-paper yield 41·3 c.c. oxygen; and after having been dried *in vacuo* at 0°, 31·2 c.c. 100 grams of dried and deoxidized hæmoglobin removes from water, saturated with oxygen between 0° and 20°, 133 c.c. oxygen at 0° and 1,000 mm. pressure (PREYER)—that is, 1 gram can combine with about 1·3 c.c. of oxygen. The *combination, however, is so loose* that the hæmoglobin easily parts with its oxygen to bodies possessing a greater affinity for it than the hæmoglobin itself; it can therefore be completely extracted *in vacuo* or by placing the blood in an atmosphere of carbonic oxide.

As to the carbonic acid gas, a varying but presumably a small proportion is in a state of solution, while the rest is in loose combination, associated probably with some salt or salts in the serum, the condition of the combination appearing to be determined in some way by the action of a constituent of the corpuscles. The serum of dog's blood contains about 35·2 per cent. carbonic anhydride, 2·24 per cent. nitrogen, and 0·26 per cent. oxygen (PFLUGER). With what salt exactly the carbonic acid is combined is doubtful—whether with soda as bicarbonate, or with sodic phosphate, etc.; some authorities even being of opinion that a portion of the gas is combined with the corpuscles, and the rest partly in a state of combination and partly in a state of solution in the plasma.

The *degree of pressure* has a considerable effect on the amount of gas present in the blood, particularly the quantity of oxygen, as a reduction of the pressure to half an atmosphere is said to reduce the oxygen to half its normal amount.

According to BERT the proportion of the gases in the arterial blood of a dog is—

	O.	CO_2.	N.
At 1 atmosphere	20·2	37·1	1·8
" 5 atmospheres	23·7	35·5	6·7
" 10 "	24·7	37·9	9·8

Changes in the Blood Gases in Respiration.—1. The blood in passing through the lungs takes up 8 to 12 vols. per cent. of oxygen; its reduced hæmoglobin is thus in great part converted into oxyhæmoglobin. This excess of oxygen in the arterial blood is given up to the interstitial fluids of the body, in which the oxygen tension is very low. How much oxygen is present in the residual air filling the air cells of the lungs it would be difficult to say, but we may safely assume that it does not fall below 10 per cent. The tension of oxygen in the arterial blood is about 4 per cent. and in the venous about 3 per cent. (in the arterial blood of the dog its average is 3·9 per cent., and in the venous 2·9 per cent.), and therefore the difference in tension will be sufficient to lead to a rapid interchange or equalization of tension.

2. The blood having become charged with carbonic acid by its interchanges with the interstitial fluid of the tissues, in which the carbonic acid is in a high state of tension, parts with its excess of carbonic acid at the lungs. Whether this separation is more than a simple case of diffusion it is difficult to say, but the tension of the carbonic acid in the venous blood is much higher (5·4 per cent. in the dog) than that of the carbonic acid in the residual air.

Some assume the occurrence of a temporary increase of carbonic acid tension in the lung, resulting from the action of the corpuscles, the pulmonary epithelium even having been assumed to possess an eliminating function.

How the Constitution of the Blood is affected.—**The constitution and characters of the blood are modified considerably according to circumstances. Normal influences alone will here be considered.**

I. (*a*) ***Difference between Arterial and Venous Blood*** (Gorup Besanez).

Physicial characters and chemical constituents.	Arterial blood.	Venous blood.
Temperature	about 1° higher.	lower.
Color	brighter, and not dichroic.	darker and dichroic.
Gases	relatively more oxygen.	relatively more carbonic acid.
Water	more.	less.
Fbrin	"	"
Hæmoglobin	less.	more.
Albumen	no constant difference.	
Fats	" "	
Extractives	more.	less.
Urea	less.	more.
Salts	more.	less.
Sugar	"	"

Although arterial blood has proportionally fewer corpuscles than venous blood, yet those of arterial blood are said to be richer in coloring matters and salts, but poorer in fatty matters than the corpuscles of venous blood (Lehmann).

(*β*) ***Characteristics of Portal and Hepatic Blood*** (C. Schmidt).

Constituents.	Portal blood.	Blood of hepatic vein.
Water	more.	less.
Plasma	"	"
Salts	"	"
Fats	"	"
Moist corpuscles	less.	more.
Extractives	"	"
Fibrin	present.	absent.
Sugar	absent, or only in traces.	abundant (only in traces —Pavy).

According to Drosdoff in portal blood there is more hæmoglobin and sodic phosphate and less cholesterin and lecithin than in hepatic blood; further, in the portal blood the proportion of the corpuscles to the plasma is 57–60 per cent. to 40–43 per cent., while in the hepatic venous blood the corpuscles form 74 to 77 per cent. and the plasma 23 to 26 per cent.

Blood of the portal vein coagulates more rapidly than that of the *right ventricle*, and its serum is reddish; it contains more water and serum albumen, and is also more charged with fatty bodies, extractives, and salts than the *blood of the jugular vein*.

(*γ*) *Splenic Venous and Placental Blood.*—The *splenic venous blood* contains more water and fibrin than venous blood generally; its red corpuscles are diminished and its pale corpuscles increased, and it is comparatively rich in cholesterin. The *blood of the fœtal placenta* is poor in fibrin and albumen, rice in albuminates, and while containing less solids than the maternal blood it is richer in urea.

II. *Influence of Sex and Age.*

(*a*) Human Blood (Becquerel and Rodier).

Constituents.	Men.	Women.
Water	77·90	79·10
Solids	22·10	20·90
Fibrin	0·22	0·22
Hæmoglobin	13·45	12·17
Albumens	7·60	7·60
Cholesterin, lecithin, and fats	0·16	0·16
Extractives and salts	0·68	0·74

(*β*) Human Blood (Gorup Besanez).

Constituents.	Men.	Women.	Children.	Old age.
Water	less.	more.	less.	more.
Fibrin	—	—	"	"
Corpuscles	more.	less.	more.	less.
Albumens	less.	more.	"	"
Fats	"	"	—	—
Extractives	"	"	more.	less.
Salts	"	"	less.	more.

The solids in the blood of a new-born child are nearly twice as great as those of an adult's blood, but in adults the ash is more abundant than in young animals.

(*γ*) In *pregnancy* the water is increased and the corpuscles diminished; at the period of parturition there is only about 11·3 per cent. corpuscles instead of 13·5 per cent.; after parturition the corpuscles increase. During pregnancy the fibrin is increased, especially in the last three months (0·35 to 0·48 per cent.); the albumens are slightly diminished, and the fats and phosphorized bodies increased.

III. *Influence of Food* (Gorup Besanez).

Constituents.	During digestion.	Continued hunger.	Flesh diet.	Vegetable diet.	Diet rich in fat.	Bread diet.	Diet rich in salts.
Water	diminished.	increased.	diminished.	increased.			
Fibrin	slightly increased.	diminished.	increased.	diminished.			
Colored corpuscles.	increased.	"					
Pale corpuscles	"	"					
Albumens	"	"	—	increased.			
Extractives	"	"	increased.	diminished.	—	sugar increased.	
Fats	"	"	—	increased.	increased.		
Salts	"	increased.	increased.	diminished.	—	—	increased.

As to the hæmoglobin, in dogs fed with a rich nitrogenous flesh diet the mean of hæmoglobin = 13·75 per cent.; in dogs fed with a non-nitrogenous diet the mean of hæmoglobin = 9·5 per cent.; and in dogs fed with bread the mean of hæmoglobin = 9·4 to 10·3 per cent. An increase in the hæmoglobin has also been noticed in human blood with an improved dietary (Leichtenstein).

During digestion the constitution of the blood changes sensibly. Under alimentation the number of pale corpuscles increases greatly, and from 1 pale corpuscle to 1.500 red the proportion may rise to 1 to 300 or 500.

After much fat has been absorbed the serum of the blood may become milky. *With abundant food* of good quality the blood is generally enriched in solids; an *animal diet* diminishing its water and increasing its fibrin, extractives, and salts, particularly its phosphates and potash; a *vegetable diet* increasing its water, serine, fats, and sugar, but diminishing its fibrin, extractives, and salts, causing a predominance, however, in the salts of lime and magnesia. *Insufficient food* impoverishes the solids as well as the total mass of the blood. A deficiency of common salt causes the hæmoglobin to extravasate into the serum, and renders it less able to absorb oxygen (POGGIALE). When taken in excess it tends to accumulate in the blood.

CHAPTER II.

HÆMOGLOBIN.

HÆMOGLOBIN (**Hæmato-globulin, Hæmato-crystallin, Cruorin, Erythrocruorin**).—This is the crystalline indiffusible substance which forms the bulk of the solids of the colored corpuscles. It possesses a very complex constitution, and its percentage composition (in the horse) is—

C	53·85–54·87	N	16·17–17·31
H	7·32– 6·97	O	21·84–19·73
Fe	0·43– 0·47	S	0·39– 0·65

PREYER has assigned this formula to it: $C_{600}H_{960}N_{154}FeS_3O_{179}$. Assuming that one molecule of hæmoglobin unites with one molecule of oxygen, the molecular weight of hæmoglobin would be 14,133, which would agree well with HÜFNER'S formula, $C_{636}H_{1025}N_{164}FeS_3O_{189}$.

Preparation.—The hæmoglobin can be separated from the corpuscles by any means tending to their dissolution, as addition of water to the blood, the passage through it first of a current of oxygen and then of carbonic acid, freezing and subsequent thawing several times repeated, electrical discharges, agitation of the blood with ether, and the addition to the blood of certain salts or of crystallized bile. By any of these processes the blood is rendered transparent or laky.

Hæmoglobin crystals are obtained with difficulty from human blood, but more readily from that of the guinea pig, dog, or rat. Different methods are given, many of which the author has found effective, some more so, however, than others; but, as much depends on circumstances, one method being more convenient at one time than another, several processes will be detailed. With the blood of rats, guinea pigs, and dogs there is generally no difficulty, and in the winter season the crystals are obtained more readily than in summer.

To Obtain the Crystals in Small Amount.—1. Defibrinate some guinea pig's blood; (*a*) add to one-third of the defibrinated blood a few drops of ether, shake well and lay aside in a freezing mixture; (*b*) mix another third with one-third its volume of water, add a few drops of chloroform, shake vigorously for a minute or two, then place a drop upon a slide and expose to the air some time before covering; (*c*) place the remaining third in a thin porcelain or platinum capsule, mix it with an equal volume of cold water, then add to the mixture one-quarter its volume of alcohol, and immerse the capsule in a freezing mixture. After 24 hours the crystals are collected on a filter, redissolved in as little water as possible at 25° or 30°, alcohol added to the solution, and the whole transferred to a freezing mixture, when crystallization will soon occur. By proceeding in this way with moderate care crystals will easily be obtained.

2. Kill a white rat or mouse by inhalation of ether, place a drop of the blood, particularly that of the splenic vein, on a slide, and after having exposed it to the air for a few seconds mix it with a couple of drops of water; allow it to evaporate for a few minutes, breathing several times upon it, and then apply a cover glass: crystals will soon appear. Still larger and better crystals will make their appearance if the cover glass is surrounded with a strong solution of pyrogallic acid and laid aside for four or five hours.

A larger crop of crystals will be obtained by treating the rat's blood as in 1 c.

3. Large crystals can be obtained for microscopic examination by enclosing in capillary tubes some defibrinated dog's blood that has been exposed to the air, laying these tubes aside several days at about 37°, and then allowing evaporation of their contents to take place on slides (GSCHEIDLEN).

On a larger scale the hæmoglobin can be obtained by one of the methods that follow:—1. 500 c.c. defibrinated dog's blood are shaken some minutes with 31 c c. of ether, and then set aside in a cool place, or better in ice. After two or three days a mass of crystals will have formed, which are best separated by the use of a centrifugal machine. They are next treated in a flask with dilute spirit. After the flask has stood for some hours the blood will have solidified, and red crystalline needles will easily be seen by examining a little of the red mass under the microscope (KÜHNE).

In the absence of a centrifugal machine the crystalline mass can be spread out on a piece of porous earthenware, and placed under the exhausted receiver of an air pump. Digest the mass now in luke-warm water, and precipitate with alcohol.

Or the crystalline mass is diluted with an equal volume of a mixture of 1 part of alcohol (90 per cent.) and 4 parts of distilled water. Filter through calico, and then place the soft hæmoglobin on a porous tile in a current of cold air (BURDON SANDERSON).

To obtain a permanent microscopic preparation a little of the crystalline mass may be rapidly spread out with needles on a warmed slide, and then covered; or else treated successively with absolute alcohol and spirits of turpentine, and mounted in Canada balsam. They may likewise be mounted in potassic bichromate (2 per cent.), or, before applying the cover glass, allow the drop to dry completely, then add damar varnish and cover in the usual way.

2. Let dog's blood coagulate, divide the clot, express it through linen, and add to the expressed fluid some solution of crystallized bile in water (1 to 3). Filter at the end of 24 hours, and add to the filtrate one-fifth its volume of alcohol. Lay aside in a cool place and wash the collected crystals in weak and then in strong alcohol (KÜHNE).

3. Defibrinated blood of horse is mixed with 10 volumes of sodium chloride solution (2 per cent.) and laid aside in a cool place. In two days the clear supernatant liquid is decanted, and to the thick red deposit left behind a little water is added, and the whole then transferred to a flask. Here it is shaken up for some time with an equal volume of ether, when the globules dissolve; the ether is decanted after standing, and the laked blood filtered and treated with quarter its volume of alcohol at 0°. It is to stand aside in a freezing mixture for several days, when crystals of hæmoglobin can be separated by filtration (HOPPE SEYLER).

4. Defibrinated horse's blood is laid aside in a tall cylinder; after some time the serum is removed with a pipette, and the mass of corpuscles transferred with

the addition of a little water to a flask, where some ether is to be added to it, the flask well shaken and then set aside. In a few hours pour off the layer of ether, and treat the mass again with more ether exactly in the same way. The watery residue is next thrown upon a plaited filter, and the filtrate collected in a cylinder surrounded by ice. To this about one-fourth its volume of alcohol (80 per cent.) that has been cooled down to 0° is added, and the mixture thoroughly shaken in a large flask, which is afterwards inserted from 24 to 48 hours in a freezing mixture of ice and salt. The crystals that separate are to be collected on a cooled filter, rapidly washed several times with a cooled mixture of spirit (1) and water (4), and then squeezed gently to express as much fluid as possible. To purify the crystals dissolve them in a little water at 30° to 40° over a water bath, filter rapidly into a cooled cylinder, add of alcohol a quarter the volume of the filtrate, and repeat the process detailed above.

The temperature all the time, except when the mass is being dissolved over the water bath, must not be allowed to rise above 0°; otherwise some of the hæmoglobin will be lost; and accordingly the process is best performed in cold weather.

5. *From Clot.*—The blood is allowed to coagulate, and then kept for 24 hours in a cool place, when it is to be dried, washed with ice-cold water, cut into little bits, and again washed with iced water; now allow it to freeze inside a freezing mixture, next rub it up in a shallow mortar, and transfer the powder to a filter, where it is to be washed with water at 0° until the filtrate gives no precipitate with mercuric chloride. Now extract the mass with water at 30° to 40°, and collect the filtrate in an ice-cooled cylinder. After having ascertained with a small specimen of the filtrate how much spirit can be added without a precipitate occurring, mix with the rest of the filtrate the estimated quantity of spirit, and lay the mixture aside in a cool place. When the crystals separate they are to be washed with water at 0°, to which a little spirit is to be added at first, until the washings give no precipitate with mercuric chloride, silver nitrate, or plumbic acetate. The washing had best be done by decantation, and the washed mass is left to crystallize in a freezing mixture.

It is sometimes possible to obtain crystals by leaving the clotted blood in a cool place for two or three days, and to a little of the fluid squeezed from it adding a drop or two of water; drops of this mixture are placed on slides, covered, and examined in a few hours.

Properties.—Hæmoglobin is capable of existing in two states of oxidation, as oxyhæmoglobin and as hæmoglobin or reduced hæmoglobin, as it is sometimes termed. These two are distinguished by their color and their absorption spectra, the oxyhæmoglobin solutions being of a bright scarlet, and giving two absorption bands in the spectrum between D and E, and the reduced hæmoglobin solutions being of a much darker purple tint, and giving only one broad absorption band between D and E in the spectrum. By means of oxidizing and reducing agents the one body can readily be converted into the other (STOKES). The reduced hæmoglobin, however, is not crystalline.

Oxyhæmoglobin is the only well-known proteid that readily assumes the crystalline form.

Hæmoglobin is insoluble in absolute alcohol, ether, chloroform, and benzole; readily soluble in water, particularly hæmoglobin of the blood of birds, but that of guinea pigs, squirrels, and rats is much less soluble; it is soluble also in alkaline solutions.

Its solutions do not diffuse through vegetable parchment, and are easily decomposed by exposure to the air, and will not therefore keep well; also decomposed by boiling, coagulation occurring with separation of albumen at about 64° to 68°. Even in the dry state it is likewise very liable to decompose; only its solutions in dilute alkalies containing a little albumen can be preserved for even a short time.

It plays the *rôle* of a weak acid, its watery solutions having a feeble acid reaction, and accordingly its very dilute alkaline solutions possess considerable stability. Its strong affinity for oxygen has already been referred to.

Hæmoglobin solutions are precipitated by alcohol, acetic acid, the mineral acids, mercuric nitrate, and potassic ferrocyanide; mercuric chloride gives a dirty grayish red precipitate, and silver nitrate a brown solution; it likewise gives the protein reactions. The acids, as well as alcohol, while precipitating also decompose it.

Hæmoglobin Crystals.—Although hæmoglobin is a colloid, it crystallizes in all vertebrates, but in some more readily than in others; these crystals are formed with great difficulty from the blood of the pig, ox, or frog, with some difficulty from the blood of sheep, men, rabbits, etc., easily from that of the dog or cat, and very easily from that of the guinea pig or rat.

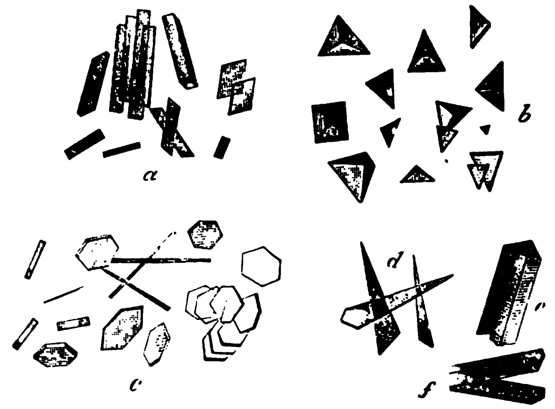


FIG. 19.—CRYSTALS OF HÆMOGLOBIN.

a, prismatic and rhombic, from human blood—somewhat similar in hare's blood; *b*, irregular rhombic tetrahedra, from blood of guinea pig; *c*, six-sided tables from blood of mouse—somewhat similar in the squirrel; *d*, needles from lark's blood; *e*, *f*, elongated four-sided needles, from blood of cat and dog.

These crystals belong mostly to the rhombic system, forming long four-sided prisms in dogs, tetrahedra in guinea pigs, and rhombic tables and prisms in man and the horse.

It is stated by H. STRUVE that freshly prepared blood crystals which have been rendered insoluble by treatment with alcohol are decolorized by ammonia or chlorine water without undergoing any change in their crystalline form. Hence he concludes that the blood crystals consist essentially of globulin mixed with a minute quantity of the red coloring matter of the blood.

Absorption Spectra.—Diluted arterial blood or a dilute solution of oxyhæmoglobin gives a double absorption band between D and E, a solution containing even 0·05 milligram dissolved in 5 c.c. water showing the two stripes. Of these two the narrow one towards D is the more intense, and is the only one visible in very dilute solutions.

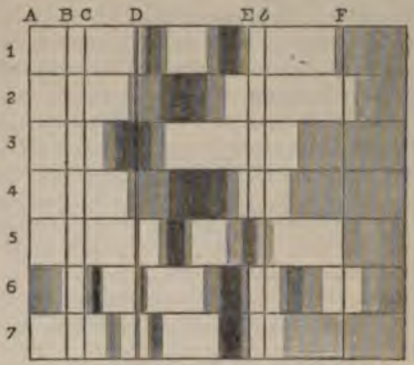


FIG. 20.—ABSORPTION SPECTRA OF BLOOD.

1. Oxyhæmoglobin. 2. Reduced hæmoglobin. 3. Alkaline hæmatin. 4. Alkaline hæmatin decomposed with potassic cyanide or potassic cyanhæmatin. 5. Alkaline solution of reduced hæmatin (corresponding nearly to hæmochromogen). 6. Hæmatoïn (prepared by the action of an ethereal oxalic acid solution on hæmoglobin—PREYER)—corresponding nearly with iron free-acid hæmatin, the band to the extreme right of the latter, however, lying more towards F. 7. Methæmoglobin in alkaline solution (JÄDERHOLM).

Reduced hæmoglobin gives but one broad and comparatively faint band, that is darkest in a position intermediate to the situation of the oxyhæmoglobin stripes, but extending also in a less intense form a little to the red side of D.

Ordinary diluted venous blood, will also give the two bands of oxyhæmoglobin, showing that there is still a large amount of this body contained in venous blood; and as these are much more distinct than the faint band likewise faintly visible and due to the large amount of reduced hæmoglobin present, the latter in not easily recognized.

Besides giving the absorption bands, part of the rest of the spectrum is shut out; thus with moderately dilute solutions of oxyhæmoglobin part of the red end of the spectrum is absorbed, and a larger part of the blue end; with the reduced hæmoglobin, on the other hand, less of the blue end is absorbed and more of the green.

Carbonic oxide exactly displaces all the oxygen in defibrinated blood (BERNARD), taking the place of the oxygen in the hæmoglobin. The new compound crystallizes like oxyhæmoglobin. Blood so treated gives two absorption bands like those of oxyhæmoglobin, but the reduction band cannot be obtained with this blood by means of reducing agents like carbonic anhydride, etc., on account of the greater stability of the carbonic oxide hæmoglobin. A slight excess of soda also brightens blood containing carbonic oxide, while it darkens normal blood.

Nitric and nitrous oxide also unite with hæmoglobin, and with *sulphuretted hydrogen* a sulphur combination of hæmoglobin is formed.

Derivatives.—Oxyhæmoglobin is decomposed by dilute acids or alkalies, or by the action of heat, into a proteid, *globin* or *globulin*, and a ferruginous pigment, *hæmatin*, of which about 4 per cent. is obtained for about 96 per cent. of the globulin bodies.

A watery solution of oxyhæmoglobin soon changes color, and gives rise to a new body, *methæmoglobin*, which is said to be occasionally met with in cysts and in the blood after the inhalation of amyl nitrite. By the addition of some freshly prepared potassic permanganate solution to a hæmoglobin solution

methæmoglobin, and later hæmatin, are obtained; nitrites act similarly. Indeed, oxidizing substances are said to change oxyhæmoglobin first of all into methæmoglobin. This body, about which some doubt exists, is said to be soluble in water, but insoluble in alcohol and ether; it is split into hæmatin and an albuminous body by acids and alkalies, and gives an absorption band in the red between C and D. This body was first described by HOPPE SEYLER, but he afterwards regarded it merely as an intermediate stage in the decomposition of hæmoglobin into hæmatin and proteids. JÄDERHOLM, however, regards it as existing as a definite body, a *peroxyhæmoglobin* which in an alkaline solution exhibits three bands in the spectrum.

A solution of oxyhæmoglobin heated to 100° decomposes, and a red precipitate occurs, in which *hæmochromogen* is described as present; and by treating reduced hæmoglobin with acids or alkalies in the absence of oxygen it is also obtained (this corresponds to the *reduced hæmatin* of STOKES); further, when decomposed with dilute oxalic acid, beside the albumen precipitate thrown down, *hæmatoporphyrin* is formed (HOPPE SEYLER).

Proportion of Hæmoglobin present in Blood.—Hæmoglobin may be said to form a little more than 12 per cent. of the blood, and about $\frac{12}{13}$ of the solid constituents of the corpuscles. Taking the proportion present in a new-born child as 100, the following numbers (LEICHTENSTEIN) will express the proportions present later in life:—

½ to 5 years = 55 per cent.
5 " 15 " = 58 "
15 " 25 " = 64 "
25 " 45 " = 72 "
45 " 60 " = 63 "

The blood of the new-born, we see, is therefore richer in hæmoglobin than that of the adult. The proportion is somewhat greater in men than in women: men, a mean of 13·58 per cent.; women, a mean of 12·63 per cent.

Assuming the average proportion of hæmoglobin present in mammalian blood generally to be 9·4 per cent., in birds the proportion is 7·8, in reptiles 4·3, in amphibia 3·9, and in fish 3·6.

According to BERT the blood of herbivorous animals acclimatized at a high elevation is richer in oxygen than the blood of similar animals inhabiting lands near the sea level, 100 c.c. of the blood in the former case containing 16·2 to 21·6 c.c. oxygen, and in the latter only 10 to 12 c.c.

In arterial blood the hæmoglobin is nearly all in the state of oxyhæmoglobin, while in venous blood most of it is in the reduced condition. The blood of a corpse only contains reduced hæmoglobin a very short time after death. In animals completely deprived of air the hæmoglobin loses its oxygen in less than a minute, owing probably to the rapid consumption of the gas by the tissues.

Tests.

I. *Ozone Test for Hæmoglobin.*—This serves also as a test for blood. Oil of turpentine long exposed to air contains ozone. If to some of this fluid we add a little freshly prepared alcoholic solution of guaiacum resin (taken from the middle of a large lump), and then lrop of blood, and shake, a dark blue color results. The hæmoglobin cts as an ozone-carrier to the resin, but it probably also serves as an zone-former. Some of the guaiacum solution should be allowed to lry on filter paper, and a few drops of blood that has been diluted 20 imes or so allowed to fall on it, when the blue reaction will appear at he margins of the drop. According to **Pflüger** the oxygen is not onverted into ozone by the hæmoglobin, the guaiacum reaction being ntirely due to decomposition of the hæmoglobin.

This test can be applied to a *dried blood stain*. The stain is moistened, and then after a time washed in a little water. To the decanted liquid add a few drops of freshly prepared tincture of guaiacum and a little ozonized ether; the mixture immediately assumes a blue or greenish blue tint.

II. *Absorption Spectra of Hæmoglobin.*—1. Some drops of blood or of a dilute solution of hæmoglobin are added to a small test tube nearly filled with water. This is then brought in front of the slit of an ordinary spectroscope, and examined with bright daylight or by means of a good lamp. With a microspectroscope, such as that of **Browning** or **Zeiss**, the bands can be still better seen. A vascular membrane such as the web of a frog's foot or the tongue of the same animal may be employed to show the spectrum of living blood.

These two bands in the yellow and the green, between D and E, have already been referred to, and are characteristic of oxyhæmoglobin; they are visible in a layer one centimetre thick of a solution containing $\frac{1}{100}$ per cent.

2. Treat the blood or hæmoglobin solution with a reducing agent, such as some drops of ammonium sulphide or of an ammoniacal solution of stannous or ferrous tartrate, prepared by dissolving ferrous sulphate or stannous chloride in water, and then adding in succession a little tartaric acid and excess of ammonia; as the result the two stripes disappear, and the single broad band of reduced hæmoglobin takes their place, the darkest point occupying the interval between the position of the two preceding bands, but its lighter margins extending considerably on each side.

3. Shake up some defibrinated blood with carbonic oxide in a test tube, and examine spectroscopically; two bands will also be seen, but situated a little more to the right than those of oxyhæmoglobin.

Allow a moderately dilute solution of hæmoglobin to stand for some time, and it will attain a brownish tint and an acid reaction; it also becomes precipitable by acetate of lead, which does not throw down hæmoglobin; and it gives an absorption band in the red between C and D.

If to a dilute solution of blood a crystal of pure potassic permanganate is added, and the solution then examined with the spectroscope, a band will be seen in the orange, and a second in the position of the broader oxyhæmoglobin band, and a third between E and F. This is stated to be due to the presence of methæmoglobin.

III. *Additional Properties.*—1. If a watery solution of hæmoglobin is boiled it will be decomposed into albumen and hæmatin, a brownish red coagulum separating. The same decomposition is effected by the use of strong acids or alkalies.

2. A drop of blood or a piece of rag that has been stained with it is to be placed in a test tube and shaken up with a little distilled water after having soaked for upwards of an hour. A few drops of ammonia are then added, the color being unaffected thereby, and the solution boiled: a turbidity will be produced, of a dirty gray color; on the addition of a drop or two of caustic potash the turbidity will disappear, and the solution will be green by transmitted and red by reflected light.

CHAPTER III.

ESTIMATION OF HÆMOGLOBIN.

This is effected (1) by the estimation of its iron, (2) by titration of the blood with sodic hyposulphite, (3) by shaking the blood with carbonic oxide, etc., (4) by the comparison of a very diluted blood with a solution of blood or hæmoglobin of known strength, and (5) by means of the spectroscope. The estimation from the amount of iron contained is very troublesome, and extremely liable to error unless great care is taken. It will not, therefore, be referred to here, but only the comparisons of color and spectroscopic methods will be detailed.

I.—*The Volumetric Color Method.*—Here the determination is made by a comparison of the tints of a blood solution and of a standard solution of hæmoglobin, or of a standard colored substitute.

(*a*) *After* Hoppe Seyler.—Prepare hæmoglobin in the winter from dog's or guinea pig's blood, purify it by recrystillization, dissolve it in water 0°, and filter. To ascertain the strength of the solution, evaporate 20 c.c. at 110°, and weigh the residue over sulphuric acid. The standard solutions are to be kept in sealed tubes.

20 grams of the defibrinated blood to be tested are made up to 400 c.c.

Process.—Take two small vessels with parallel walls 1 centimetre apart; into the one pour 10 c.c. of the hæmoglobin solution, and dilute it with 60 c.c. water; and into the other 10 c.c. of the blood solution. The two little vessels are then to be placed side by side upon white paper, and their depth of color observed; distilled water is next to be added to the blood solution by means of a graduated pipette until it acquires exactly the same tint as the hæmoglobin solution. When the two colors are indentical we note the number of c.c. of water which have been required. The experiment should be repeated, diluting the 10 c.c. of hæmoglobin solution with 80 or 100 c.c. of water instead of 60 c.c.

Let us suppose now that the normal solution of hæmoglobin contains 0·00145 gram hæmoglobin in each c.c., and that it requires an addition of 38 c.c. water to the 10 c.c. of the diluted blood to obtain the same depth of color as that of the standard hæmoglobin solution; then

$$10 : 10 + 38 = 400 : x = 1920.$$

That is, the 400 c.c. of blood solution must be diluted to 1,920 c.c. to attain the tint of the standard hæmoglobin, and, as 1 c.c. of this contains 0·00145 gram hæmoglobin—

$$1 : 0{\cdot}00145 = 1920 : x = 2{\cdot}784.$$

The diluted blood will accordingly contain 2·784 grams, and therefore the defibrinated blood = 2·784 × 5 = 13·920 per cent. hæmoglobin.

(*b*) As the standard solution of hæmoglobin is both troublesome to make and keeps badly, it is more convenient to use as our standard of comparison a solution of carmine or picrocarmine to which a little phenol and glycerin have been added; this is graduated by comparison with a standard hæmoglobin solution. The colored solution is readily prepared by dissolving 1 gram pure carmine in a little water and ammonia with the aid of heat, adding the solution to 100 c.c. of a boiling saturated solution of picric acid, evaporating to dryness, dissolving the residue in 100 c.c. water, and filtering the solution thus formed. With this solution any depth of color can readily be imitated.

Dr. GOWERS uses as his standard of comparison a solution of 1 per cent. of blood in water, and, so as to have a stable standard, imitates the exact tint of this with some glycerin jelly colored with carmine or picrocarmine.

Process.—20 c.c. of the blood to be tested, measured by means of a capillary pipette, are added to a glass cylinder like that containing the colored jelly, and to which a few drops of water have previously been added. Distilled water is then added drop by drop, with continual agitation, until the same tint is obtained as that of the standard of comparison. The amount of water added indicates the hæmoglobin. The normal standard marks 100 degrees of dilution, so that if the blood we are testing gives the same tint when diluted, say 40 times, then it contains only 40 per cent. of the normal amount of hæmoglobin.

Only approximative results, it may be said, are thus obtained.

II. *Determination of Hæmoglobin by the Spectroscope* (PREYER).—This process is the most accurate, and its only difficulty consists in the preparation of the standard solution; but when this has been done, and the value of κ once ascertained, subsequent experiments will merely require exactly the same conditions to be observed in examining the blood as were pursued with the hæmoglobin.

Principle of the Process.—Concentrated solutions of hæmoglobin are quite opaque to all but the red rays of the spectrum; less concentrated solutions, however, allow, in addition to the red and orange, a part of the green to pass. If now a solution of the hæmoglobin is made of such a density as to permit the green to pass, and if the amount of hæmoglobin present in such a solution is determined, we possess a standard of comparison. To determine the hæmoglobin in a specimen of blood it will therefore be necessary to defibrinate it, and to dilute a measured quantity of it until it allows the green of the spectrum to appear when examined with a spectroscope.

Preparation of a Standard Solution.—A little glass vessel with two of its parallel walls 1 centimetre apart is to be placed close in front of a lamp in a darkened room. Into it is poured 1 c.c. strong solution of hæmoglobin, and with a spectroscope the light is examined through the layer of fluid. If sufficiently concentrated no light passes. Distilled water is now carefully added from a finely graduated pipette until the green just begins to appear in the spectroscope. The diluted solution of hæmoglobin in the little vessel is then poured into a small weighed porcelain capsule, and its weight taken; the solution is next evaporated over a water bath to complete dryness, and weighed again. We thus obtain the amount of hæmoglobin present, and can calculate therefrom the percentage of the solution.

Determination of Blood.—With all the arrangements exactly as before, about 0·5 to 0·8 c.c. of fresh defibrinated but unfiltered fresh blood that has been well shaken in the air is poured into the little vessel with parallel walls. Drop by drop distilled water is let fall into this from a finely graduated pipette until the green begins to be seen in the spectroscope.

If κ = the percentage of a hæmoglobin solution allowing the green to pass, v = the volume of water in c.c. added to the blood until the green appears, b = the volume of the blood in c.c., and x = the percentage of the hæmoglobin in the blood, then

$$x = \frac{\kappa(v+b)}{b};$$

or if the quantity of blood employed, b, be equal to 0·5 c.c.,

$$x = \kappa(1+2v).$$

Suppose now that $\kappa = 0{\cdot}8$ per cent. hæmoglobin, the quantity of blood employed = 0·551 c.c., and the volume of water added = 8·54 c.c., then

$$\frac{0{\cdot}8(8{\cdot}54+0.551)}{0{\cdot}551} = 13{\cdot}19 \text{ per cent. hæmoglobin.}$$

The author has obtained fairly accurate results by using standard solutions of normal blood instead of hæmoglobin, and also by repeating the experiments in a darkened room, with the same *intensity of light*, etc., as was primarily used in determining the value of κ.

Pathology.—Taking the normal amount of dry hæmoglobin as 12·7 per cent. (QUINQUAND), in chlorosis it may sink to 7·2 to 4·6 per cent.; in cancer, to 5·7 to 4·3 (in fibrous tumors and cysts, while the hæmoglobin may fall to a mean of 8 per cent., in cancerous tumors it may be as low at 4 to 3·8 per cent.); in leukæmia, to 6 per cent.; first stage tubercle, to 10 per cent., third stage from 10·6 to 4·8 per cent.; in severe typhoid fever (about the twelfth day), to 11·5 per cent.; and in acute atrophy of the liver, to 8·1 to 6·7 per cent. In cholera it often rises to 15 to 20 per cent. In chronic anæmia HAYEM has noticed that there is less hæmoglobin in the corpuscles themselves than in the normal condition.

CHAPTER IV.

HÆMATIN.

HÆMATIN, $C_{34}H_{35}N_4FeO_5$ ($C_{32}H_{32}FeN_4O_6$—THUDICHUM).—This is a bluish black amorphous body, forming a reddish brown powder that can be heated without decomposition to 180°, and which, when burnt, leaves pure oxide of iron behind. It is insoluble in water, alcohol, ether, and chloroform, but easily soluble in the alkalies or alkaline carbonates; it is with difficulty soluble in acetic or the mineral acids, and hydrochloric appears to be the only one of these that dissolves it without its iron separating. Solutions of hæmatin are dichroic, being reddish brown in a thick and olive green in a thin layer. Like hæmoglobin, hæmatin exists in an oxidized and a reduced condition, freshly reduced hæmatin passing rapidly back into the ordinary form.

Preparation.—1. Dilute defibrinated blood with a large quantity of 10 per cent. sodic chloride solution. The globules swell and separate from the serum. They are washed with saline solution, dried at a low temperature, and then rubbed up with 15 to 20 times their weight of glacial acetic acid. Warm over a water bath till the solution is complete; then dilute with five or six volumes of water and lay aside for several weeks, when crystals of chlorhydrate of hæmatin separate. Decant, purify the crystals by redissolving them in acetic acid, and dilute as before with five to six volumes of water. Pure hæmatin can be obtained from these crystals by dissolving them in ammonia, evaporating the solution to dryness, and heating the residue to 130°; next digest the dry mass for several days with absolute alcohol at 50°, filter, and the red alcoholic solution will, on evaporation, yield pure hæmatin.

2. Digest coagulated blood, or the separated corpuscles, with alcohol containing sulphuric acid, warm gently over a water bath, and filter rapidly: a dark brown solution of hæmatin is obtained.

3. Defibrinated blood is shaken with twice its volume of ether containing quarter its bulk of alcohol. Decant after 24 hours, and exhaust the coagulum with ether containing 2 per cent. oxalic acid. The hæmatin is precipitated from this by adding to it ether charged with ammonia, and it is lastly washed with water, alcohol, and ether.

Derivatives.—By the action of most of the acids—sulphuric acid, for example—a solution of hæmatin is decomposed, and *iron-free hæmatin* (apparently identical with *cruentin*, *hæmatoporphyrin*, and *acid hæmatin*) is thrown down, hydrogen at the same time being disengaged, and ferrous sulphate (if the decomposing acid has been sulphuric) formed. This new body is regarded by HOPPE SEYLER as being of the same nature as bilirubin. PREYER'S *hæmatoïn* is also very similar to this iron-free hæmatin, like it containing no iron. If some blood or strong hæmoglobin solution is shaken up with an equal volume of ether to which a little acetic acid has been added, and the dark-colored ethereal solution decanted and allowed to evaporate over caustic alkali, stellate brown needles will be obtained of this body.

Absorption Spectra (see p. 202).—1. A dilute alkaline solution gives a faintly marked band at D, with much absorption of the blue end of the spectrum. By increasing the strength of the solution the band extends towards C, and with still further concentration broadens also towards E, the red end of the spectrum as well as much of the blue end being absorbed. The same spectrum is obtained with solutions of blood or hæmoglobin that have been rendered distinctly alkaline, and then allowed to stand some time.

2. If to some of the above solution of blood or hæmoglobin a little strong potassic cyanide solution is added, a broad absorption band rapidly makes its appearance like that of reduced hæmoglobin, but lying more towards E. Now treat the solution with such a reducing agent as ammonium sulphide: two bands then appear between D and E, very like in their position to the oxyhæmoglobin stripes, but neither of them touching D or E, the narrowest band being separated from D by a considerable interval (*cyanhæmatin* of LANKESTER).

3. The ethereal solution of PREYER'S *hæmatoïn*, or a solution of the *iron-free* or so-called *acid hæmatin* in alkali or in alcohol containing some sulphuric acid, gives four absorption bands—one distinct band in the red near C; two bands between D and E, of which one is a faint narrow stripe near D, and the other a broad dark band near E; and an indistinct band in the blue between *b* and F. But a slight difference

exists between the spectra of the two solutions, for the bands near C and E are broader and more distinct, and the stripe near D narrower and fainter in the hæmatoïn spectrum.

4. Oxyhæmoglobin or a blood solution, when reduced by ferrous sulphate, ammonic sulphide, or grape sugar at 40°, gives a temporary intermediate product, HOPPE SEYLER'S *hæmochromogen* ($C_{34}H_{36}N_5FeO_5$), which is apparently identical with STOKES'S *reduced hæmatin;* it gives a dark absorption band between D and E, but nearer D, and a second faint band extending from a little on the red side of E to the blue side of *b*.

This reduced hæmatin or hæmochromogen can be preserved some time in alkaline solutions if not exposed to the air, but it will decompose rapidly in acid solutions *hæmatoporphyrin* being formed.

HÆMATOIDIN occurs in yellow crystals in old extravasations. Its composition corresponds to the formula $C_{30}H_{34}N_4O_6$, which makes it homologous with bilirubin, but PREYER maintains that they are not identical spectroscopically. ROBIN regards it as hæmatin which has lost all its iron and acquired an atom of water.

CHAPTER V.

HÆMIN.

HÆMIN (Teichmann's Blood Crystals), $C_{34}H_{35}N_4FeO_5.HCl$, has not been found preformed in animal bodies; it is a bluish black or dark brown, metallic-looking, very stable crystalline powder. In dilute acetic acid, water, alcohol, ether, and chloroform it is almost insoluble, but soluble in hydrochloric and sulphuric acids and in solutions of the alkalies and alkaline carbonates, but being decomposed in its solution.

Hæmin crystallizes in numerous forms belonging to the rhombic system ; these are most generally small brown or almost black rhombic prisms or tables.

Preparation.—1. On a small scale crystals of hæmin can be obtained by proceeding as in the first of the tests given below.

2. To obtain it in bulk, separate the corpuscles from a quantity of blood, and having decanted the serum, dry the corpuscles over a water bath at 50°; add a sufficiency of acetic acid to form a solution with the aid of heat. This having been effected mix the solution with five times its volume of water, and set the whole aside in a cylinder in a moderately cool place. At the end of several days decant and wash the crystalline residue repeatedly with water for a considerable time.

3. Boil 300 c.c. glacial acetic acid in a flask over a water bath, and add to it with frequent agitation 100 c.c. of blood. The hæmoglobin is decomposed, and both the hæmatin and globulin remain in solution. Pour the hot fluid into a beaker, and lay aside. After twenty-four hours a deposit of very small, dark blue, silky crystals occurs; these are to be washed in water by decantation and finally collected on a filter.

4. Rub up some powdered blood clot with one-fifth its weight of potassic carbonate, then digest the mixture at 45° with alcohol (93 per cent.); dilute the filtrate with its own volume of water and acidify slightly with acetic acid. The brown flocculent precipitate is to be dried, rubbed up with one-fifth its weight of sodic chloride and 20 to 30 times its weight of glacial acetic acid, and the mass digested at 60°. Separate the hæmin crystals as above.

Tests.—1. The dried blood is to be powdered, mixed with a few crystals of dried sodium chloride, and gently warmed on a glass slide; then add a few drops of glacial acetic acid and warm again; now add some fresh acid, and having applied a cover glass heat once more, when the characteristic crystals will appear. Larger crystals will be obtained by repeating the process several times; but sometimes this must be done even to render the experiment successful. When fresh blood is employed the addition of the salt may be omitted. To preserve these crystals they may be sealed up in acetic acid, or the surplus acid may be removed and replaced by Farrant's solution.

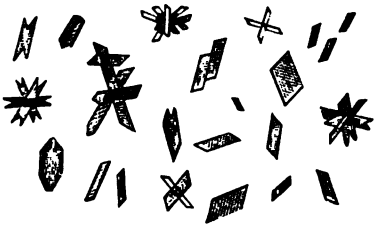


FIG. 21.—RHOMBIC CRYSTALS OF HÆMIN.

2. Take a little hæmin and dissolve it in dilute hydrochloric acid; this solution, when examined spectroscopically, gives a band in the red near C, and a second diffuse band in the broad space from E to F, but also extending towards D.

An alkaline solution is dichroic, brown with transmitted and olive green with reflected light.

CHAPTER VI.

COAGULATION.

FRESH-DRAWN blood begins to set or solidify 1¾ minute to 6 minutes after its removal from the living blood vessels, and this coagulation, as it is termed, is completed in 7 to 16 minutes (NASSE). In healthy blood the coagulation occurs slowly, but the blood of delicate persons, or of invalids, women, and children, coagulates more rapidly. This setting of the blood is due to the solidification or separation of the fibrin, which usually occurs at the surface and periphery, principally at first in the under layers of the blood, and spreading from thence upwards and outwards. The clot, the great mass of which consists of corpuscles, the amount of fibrin being very slight, takes the form of the vessel in which the blood is contained. The colored corpuscles are in greatest numbers towards the base of the clot, while the pale corpuscles, being specifically lighter, are most abundant at the surface; in certain conditions, as in hydræmia, chlorosis, and pregnancy, as well as inflammations, owing to the more rapid sinking of the colored corpuscles, or, as in horse's blood, to the slower occurrence of the coagulation, the surface may present a yellowish tint, forming the so-called *buffy coat.*

By the contraction of the fibrin threads the serum is squeezed out, and this may continue for twenty-four to forty-eight hours; but the occurrence of coagulation as well as the completion of the contraction will vary as to time, according to the condition of the blood itself and of its surroundings when withdrawn. Arterial blood, for example, coagulates more rapidly than venous blood; and coagulation may be accelerated, retarded, or prevented by alterations in the temperature or by the admixture of the blood with reagents of different kinds. Thus it is *accelerated* by moderate elevation of temperature, occurring most readily about 38°; by exposure to foreign contact, agitation, and the like, and by the addition of a small proportion of different salts. It is possible that these agencies act by favoring the disintegration of the pale corpuscles from which the ferment is derived. Irritation, in short, of every kind would appear to favor the destruction of the pale corpuscles, and thus increase the proportion of fibrin (MANTEGAZZA).

On the other hand, coagulation may be ***retarded or prevented*** by a low temperature (0°), by the addition in considerable amounts of acids, caustic alkalies, and salts such as magnesic sulphate, sodic chloride, etc.; further, the addition to the blood of sugar or gum in quantity, or of glycerin in excess, as also the passage through it of a current of ozone, delay and prevent coagulation.

Additions of water up to half the volume of the blood hasten coagulation, while larger quantities hinder it.

The slower coagulation of venous than of arterial blood is dependent not on want of oxygen, but on its richness in carbonic acid. Want of oxygen in the blood appears to hasten, whilst richness in oxygen delays coagulation (HASEBROCK).

Theories as to the Causes of Coagulation.—Without referring to the earlier theories, I shall confine myself to a brief synopsis of a few of comparatively recent date.

1. The influence of the living vessels seems to prevent coagulation during life; indeed, BRÜCKE was of opinion that the normal living walls of the vessels exerted an active influence in opposing its occurrence. The endothelial lining, however, must be in a healthy condition, for if it undergoes irritation and germination, or is broken through in any way, a clot forms over the altered region; and accordingly, as in the case of thrombi, clots may form in the living vessels. A normal relation or equilibrium, as FOSTER puts it, would seem to be maintained between the blood and its immediate investment: when this is disturbed coagulation results.

2. *Theory of Denis.*—There exists in the plasma a substance (*plasmin*) which can be separated by the addition of an excess of sodic chloride; this precipitate dissolves in water, and the solution coagulates spontaneously, separating thus into ordinary fibin and a fibrin soluble in solutions containing traces of sodic chloride. When the blood coagulates, this last fibrin remains in solution in the serum. Coagulation, according to this theory, would therefore be due to the decomposition of a body previously dissolved in the plasma.

The presence of a soluble fibrin has also been maintained by EICHWALD, MATTHIEU, and URBAIN, etc., which under certain conditions passes out of solution.

3. As soon as the corpuscles lose their vitality much of their globulin escapes from them. In the living circulating blood this globulin is contained in the corpuscles, and accordingly no coagulation occurs until it combines with other bodies normally present in the plasma. Anything, such as foreign contact, leading to an impairment of the vitality of the globule will tend to favor the discharge of its globulin, and the consequent occurrence of coagulation; while the presence of carbonic acid, neutral salts, or sugar in such amount as to render the plasma denser, or to hinder the rapidity of oxidation, will tend to retard the process (GAUTIER).

(*a*) According to SCHMIDT the presence of three bodies is necessary for coagulation to occur—*fibrinogen*, contained in the blood plasma; *fibrinoplastin*, contained in the corpuscles; and a *fibrin ferment* which cannot be found in the living blood unless, owing to some abnormal condition, it is generated by a destruction of pale corpuscles. A similar ferment is found in all protoplasmic cells, such as those of lymph, chyle, and pus, etc. Both the fibrinoplastin and the ferment, SCHMIDT affirms, are derived from the disorganization of the pale corpuscles, the fibrinogen alone being a normal constituent of the plasma. By the interaction, then, of these previously separate bodies fibrin is formed.

During life any fibrinoplastin formed by the disintegration of pale corpuscles is always being oxidized, thus tending to disappear; but if this destruction of the corpuscles is greatly increased, as by the injection of solutions of pepsin or pancreatic juice into the blood, coagulation ensues (ALBERTONI).

In addition to SCHMIDT'S *three factors* a neutral salt like NaCl requires also to be present—is, in fact, essential to the process.

Some serous fluids are wanting in the fibrinoplastic substance, and some in the ferment. The quantity of the ferment present has no influence upon the amount of fibrin formed, but it affects markedly the rapidity of the process; and the fibrin generated is less in weight than the fibrinoplastin used up, and an excess of this body is found in the serum after coagulation has occurred.

(*b*) HAMMARSTEN and FRÉDÉRICQ are of opinion that there is but one generator of fibrin, fibrinogen, which under favorable circumstances, apparently associated with the action of a ferment derivative of the pale corpuscles, is decomposed and fibrin formed.

Fibrin cannot, then, appear in a fluid devoid of fibrinogen, but without the presence of certain derivatives of the pale corpuscles it cannot be formed from fibrinogen alone. SCHMIDT'S fibrinoplastin simply favors the formation of fibrin from the fibrinogen, but its presence has no effect on the quantity of fibrinogen used up, although it has a marked influence on the amount of fibrin produced.

(*c*) HEYNSIUS believes that the colored corpuscles play an important rôle in coagulation, the chief part of the fibrinogen, according to him, being derived therefrom, although SCHMIDT ascribes the favorable action of the colored corpuscles to the ferment that comes from them.

HAYEM describes under the name of *hæmatoblasts* a series of small granular corpuscles which are very delicate in their consistency, more or less biconcave and irregular in shape, and either colorless or stained by hæmoglobin; as to their pre-existence in the living blood there may be some doubt, but HAYEM attributes to them an active share in coagulation, as they serve, according to him, as centres from which delicate threads of fibrin radiate, so that coagulation would seem to have its origin in the physico-chemical acts accompanying their decomposition.

Fibrin.—Human blood furnishes 0·1 to 0·4 per cent. dry fibrin. If fibrin is left in a moist condition in a warm place it gradually liquefies and becomes putrid, a coagulable albumen being formed as well as butyrate, valerate, and sulphide of ammonium.

LUSANNA regards fibrin as the liquefied and oxidized tissue detritus, tetanized muscle, he states, furnishing twice as much fibrin as the resting muscle; the lymph also more than blood, because it contains more of these waste products; and the arterial blood more than the venous blood, on account of the excess poured in by the lymph. (For fibrin see under Albumens, p. 113.)

CHAPTER VII.

METHODS AND PRACTICAL EXERCISES FOR THE SEPARATION, PREPARATION, OR IDENTIFICATION OF DIFFERENT BLOOD CONSTITUENTS.

1. **Albumen of Serum.**—Dilute the serum with twice its volume of water, and add very dilute acetic acid until a precipitate occurs—this is *paraglobulin;* filter, and having rendered the filtrate slightly alkaline, dialyse, and after some time concentrate the contents of the dialyser. *To separate serum globulin and serum albumen*, add to the serum a saturated solution of magnesic sulphate; the serum albumen remains in solution, the globulin being precipitated. The ser-albumen can be separated from excess of salines by dialysis.

2. **The Salts of the Serum.**—Faintly acidify the serum with acetic acid, boil for some time, and filter; the filtrate is often termed *serosity.* The precipitated albumen contains a little fat and some earthy salts, which may be removed by boiling first with alcohol and then with dilute hydrochloric acid.

The *serosity* is to be carefully evaporated nearly to dryness, when crystals of *sodic chloride* will form. Pour off the mother liquor, and having evaporated it to dryness, ignite the residue, when a white fusible ash will be obtained. To a trace of this add a drop of nitric acid, and note the evolution of carbonic acid gas; the rest of the ash is boiled in water and a little *carbonate of ammonia* added.

(*a*) *The precipitate* is collected on a filter, well washed in water, boiled in a little dilute hydrochloric acid, evaporated just to dryness, then dissolved up again in water and filtered. This solution of the precipitate contains *phosphates* and a *trace of lime.* To part of it a few drops of nitric acid and then excess of ammonia molybdate are added, and on warming gently a bright yellow precipitate of ammonio-molybdic phosphate appears. To the rest add excess of oxalate of ammonia and shake well, when oxalate of lime will be precipitated.

(*b*) The *filtrate* from the ammonic carbonate precipitate contains the alkalies, soluble chlorides, sulphates, and phosphates.

(j) To one half add a few drops nitric acid, and then a little baric nitrate, when the *sulphates* are precipitated; to the filtrate add excess of silver nitrate, which throws down the *chlorides;* and to the filtrate therefrom add dilute ammonia to neutralization, when yellow *phosphate* of silver makes its appearance.

(ij) The other half is to be evaporated to dryness, and the residue gently ignited and subsequently dissolved in water, a few drops hydrochloric acid added, and then evaporated in a capsule; sodic chloride crystallizes out in cubes. Decant the mother liquor, add to it platinic chloride and alcohol, and stir well with a glass rod, when a crystalline yellow precipitate of potassio-platinic chloride will form.

3. **Separation of Lecithin, Fats, and Cholesterin from the Colored Corpuscles.**—A clot is expressed through a linen cloth, and the fluid that exudes is to be treated with excess of ether and well shaken; the ether is separated by decantation, and the residue again extracted with more ether. The ethereal extract is then filtered and evaporated; a crystalline residue is obtained of fats, cholesterin in needles, and lecithin in little tufts. By adding water the lecithin swells up and becomes almost insoluble in ether, so that by treating the residue with the latter solvent after the action of the water the fats and cholesterin are removed.

4. **Separation of the Corpuscles.**—(*a*) Let the blood flow from the vein into a saturated solution of sodic sulphate contained in a vessel surrounded by a freezing mixture; no coagulation will occur, and the corpuscles will settle down to the bottom of the vessel. Pour off the supernatant liquid after two or three hours and collect the sediment on a filter, where it is to be washed with a solution of sodic sulphate.

(*b*) Snip off the apex of a frog's heart and let the blood flow into a solution of sugar (½ per cent.); filter rapidly; the filtrate coagulates immediately.

(*c*) Allow the blood to flow into a cold and dilute solution of magnesic sulphate (2 per cent.) and of ammonic chloride (2 per cent.) The globules sink and can be collected by filtration.

(*d*) One of the most ingenious methods is to collect some venous blood in a tube surrounded by a freezing mixture, and then subject the tube with its contents to a continuous and very rapid horizontal rotatory motion in a centrifugal machine; the globules tend to collect at the outer end of the tube (SALET and DAREMBERG).

(*e*) Collect some horse's blood in a long narrow thin glass cylinder immersed in a freezing mixture. After a couple of hours remove the fluid from the deposited corpuscles by means of a siphon, and wash the corpuscles with salt solution.

The *plasma* can also be obtained by any of these methods.

5. **Experiments with Plasma.**—(*a*) Place a little in a watch glass and warm gently, when a clot forms, owing to the coagulation of the plasmin present.

(*b*) Add to another watch glass some of the plasma, and four times its volume of distilled water: a coagulum will form after some time.

(*c*) To a third watch glass add some plasma, then a little magnesic sulphate solution (1 : 4) and about eight parts of water: no coagulation will occur until a little fibrinoplastin is added.

6. **Preparation of Fibrinoplastin and Fibrinogen.**—(*a*) Dilute a little serum with ten times its bulk of cold water, and pass a current of carbonic acid gas through it: a granular precipitate of *fibrinoplastin* is

obtained, which will settle after some time. Saturation of the serum with sodium chloride produces the same result.

(*b*) Dilute some hydrocele fluid with ten to twenty times its volume of water, and by saturating it with sodic chloride in powder, or by passing a current of carbonic acid gas through it for some time, a white slimy precipitate of *fibrinogen* is obtained.

7. **Preparation of Blood Ferment.**—Coagulate fresh ox blood by the addition of 20 volumes of alcohol (85 per cent.), filter, and after eight to twelve days decant and dry the residue over sulphuric acid; then pulverize and digest the powder with distilled water. By reprecipitating the watery solution with alcohol, and drying the precipitate again over sulphuric acid, the ferment is purified.

8. **Preparation of Fibrin Clot.**—(*a*) To a little hydrocele fluid add some serum, and after a short time a clot will form. The hydrocele fluid contains fibrinogen, and the serum fibrinoplastin and ferment.

(*b*) Prepare fibrinogen from diluted hydrocele fluid by saturating the latter with sodic chloride, and fibrinoplastin by saturating diluted serum in the same way. Now, after washing the precipitates well with a little water to remove excess of sodic chloride, they will soon dissolve when more water is added; mix the solutions thus obtained and a clot will form.

9. **Detection of Ammonia.**—This, as a rule, can only be detected in diseased conditions, particularly in uræmia and certain zymotic diseases.

Place the fresh blood in a small beaker and cover with a plate of glass, this being rendered more or less air-tight by smearing the points of contact with lard. On the under surface of this slip of glass spread out a few drops of ammonia-free dilute sulphuric acid before it is fixed down. Leave the beaker aside for an hour or so in a moderately warm room, and then test the dilute sulphuric acid with a few drops of NESSLER'S solution, when ammonia will be shown by the yellow coloration.

NESSLER'S *solution* is thus prepared: 35 grams potassic iodide and 13 grams mercuric chloride are added to 800 c.c. of water, and the mixture boiled with frequent stirring until the salts dissolve. Then a cold saturated solution of mercuric chloride in water is carefully added until the red mercuric iodide formed just begins to remain undissolved. We have now a solution of potassic iodide saturated with mercuric iodide. This is rendered alkaline and sensitive by the addition of 160 grams caustic soda, and the whole diluted up to 1 litre. A little more mercuric chloride must be added, and the mixture laid aside to settle. The *reagent* should have a yellow tint.

CHAPTER VIII.

TESTS AND CHARACTERISTICS OF BLOOD.

I. Chemical Tests for Blood.

1. Immerse a piece of linen rag in blood and dry it. Leave a cutting of this for a couple of hours in cold water, and a dingy red

solution will be obtained, some of the coloring matter also gradually collecting at the bottom of the vessel.

2. Boil a little of the solution thus obtained, and a dirty red coagulum will form. Decant the fluid, and having added to it a little caustic potash, boil, and a solution will be obtained which will be *red by reflected and green by transmitted light.*

3. Add a few drops of nitric acid to a little of the colored solution, and a brown coagulum will appear.

4. Boil a slip of the stained rag in water to which some tannic acid has been added, and it will become black or gray colored.

5. Boil another slip with dilute hydrochloric acid, and add a few drops of potassic ferrocyanide: a blue precipitate appears, indicating iron.

6. Add to a little blood twice its volume of caustic soda (sp. gr. 1·3), and a flocculent greenish brown precipitate is obtained, which gradually dissolves; if now a small stoppered bottle is filled with the solution and laid aside, it will after a time assume a violet color.

II. Practical Exercises with the Spectroscope.

1. *Oxyhæmoglobin.*—Examine a dilute solution of blood or hæmoglobin about two-fifths of an inch thick spectroscopically, and the two bands between D and E will be seen; note that the band near D is narrower, darker, and better defined than the other.

2. *Spectroscopic Examination of the Circulating Blood.*—Bring two of the fingers together in front of a bright light in such a way as to allow a faint rosy light to pass through; examine this last with a spectroscope, and the two absorption bands of arterial blood will be seen. Then apply an elastic ligature to the two fingers, and on examining as before it will soon be noticed that instead of the two absorption bands of oxyhæmoglobin the single band of reduced hæmoglobin makes its appearance.

3. ***Reduced Hæmoglobin.***—Add to a little blood or hæmoglobin solution some reducing agent, as ammonic sulphide, protochloride of tin, or the ferrous sulphate mixture (p. 205). Examine rapidly, and a single broad band occupying about three-fourth of the space between D and E will be seen.

4. ***Hæmatin.*** (*a*) *Alkaline Hæmatin.*—Add a little ammonia or caustic potash to a solution of blood or hæmoglobin; a broad band appears between C and D, but nearer D; with concentrated solutions, say of baric hydrate, the band extends more on each side, reaching on the blue side nearly halfway between D and E.

(*β*) *Acid Hæmatin.*—Add some drops of acetic acid to the small tube or vessel containing a moderately concentrated solution of blood or hæmoglobin. Sometimes it is advantageous to add in addition a volume of ether equal to that of blood. On examination several bands are to be seen, but one distinct black band in the red is to be looked for, almost coinciding with the line C, and extending somewhat on each side. The position and character of this band vary more or less according to the acid employed. PREYER, indeed, partly for this reason divides these acids into four groups. With formic acid, for example, the band lies a little more to the right than with acetic or phosphoric acid, and with oxalic acid still further; but the strength of the acid also causes a variation.

(γ) *Reduced Hæmatin.*—Treat the solution of acid hæmatin used in the previous reaction with a ferrous salt, and two new bands appear, one beginning near D and extending halfway between D and E, and the other stretching on each side of E.

III. Detection of Blood in Spots, Stains, &c.

A. *By the Microscope.*—If the blood is still liquid place a drop of it on a slide under a thin cover glass, and if it cannot be examined at once surround the margin of the cover glass with a little melted paraffin or wax.

Note the shape and diameter of the corpuscles, and whether nucleated or not.

If the blood spot is dry it must be softened with iodized serum (prepared by adding tincture of iodine to amniotic fluid until the latter acquires a faint yellow tint, or to an artificial serum consisting of water 270, sodic chloride 0·4, and albumen 30), or with sodic chloride solution (three-fourths per cent.), or sodic sulphate solution (one-half per cent.), or saturated watery solution of arsenious acid. Recent blood stains are bright red, older stains of a reddish brown. With recent stains softening occurs rapidly, but an old spot may require days. By means of a capillary tube some of the colored fluid is to be transferred, as before, to a slide and examined. Thin threads of fibrin may be seen, and by the addition of acetic acids these are rendered more distinct, on account of their swelling up and assuming a gelatinous aspect.

As it is very important to discover the presence of the corpuscles, an effort should always be made to find them.

B. *By Chemical Examination.*—*To obtain a solution of the blood*, especially if it is in the form of an old dry stain, it may be necessary, in case the blood is not removed by soaking the stain in water, to seal up the piece of stained rag in a stout glass tube containing a little water; this tube is then suspended for an hour in oil at a temperature of about 150°.

A solution of arsenious acid serves well as a blood solvent, also a watery solution of borax. When blood is diluted with water it may be precipitated with acetate of zinc, by which means it may be detected even in dilute solutions.

(*a*.) *The Guaiacum Test.*—Add to a solution of the blood some tincture of guaiacum and a little ozonized ether; the former should be freshly prepared (p. 205), and the ozonized ether can be made by adding oxygenated water to pure sulphuric ether.

The test may also be thus applied: Moisten the spot with water and cover it with several folds of white blotting-paper that gives no reaction with the guaiacum. Now press the paper very firmly down upon the suspected spot; if blood is present the paper will generally acquire a yellowish red or brownish stain. Cut this stain into two or three strips;

treat one with ammonia, and note if a scarlet or greenish tint is obtained; moisten another strip with spirits of turpentine that has been exposed to the air, and add a drop of the tincture of guaiacum, and to the third slip some drops of the guaiacum tincture and ozonized ether. Note if a pale or indigo blue appears in a few minutes in the last two slips. The presence of nasal mucus, saliva, and pus interferes with this test.

(*b*) The stained parts are to be scraped, washed, etc., and a solution prepared with as little water or borax solution as possible.

(j) Drops of this solution are then to be placed on watch glasses or on slides, and to be tested in turn with drops of the following solutions: nitric acid, acetic acid and ferrocyanide of potassium, and tincture of nut gall. All these reagents effect a precipitation, and the whitish flocculent opalescence produced is easily recognized under the microscope.

(ij) To a little of the solution add a drop of ammonia: the red color of blood is not altered; vegetable reds, however, become blue.

(iij) Dissolve a little of the stain or clot in boiling caustic potash: the stain loses its color and the solution obtained will appear reddish by reflected and greenish by transmitted light, and will give a precipitate with nitric acid.

(iv) To a little of the filtered solution add tungstate of soda solution strongly acidulated with acetic acid, and a reddish brown precipitate appears. If this precipitate is dissolved in ammonia a reddish green dichroic solution is obtained.

C. *By the Spectroscope.*—This method requires considerable care, and although it is very characteristic the results are not always easy to obtain unless the blood is sufficient in quantity. It is also advisable to use a spectroscope with a scale, and to note the exact position of the bands. Both the oxyhæmoglobin bands are seen faintly with $\frac{1}{20}$ per cent. solutions of hæmoglobin (PREYER). The solution, if too dilute, may be evaporated on a watch glass and the dry residue examined. This same dry residue can then be used for the preparation of hæmin crystals, as in D.

(*a*) The spots or stains are scraped off and digested in water to which a little ammonia has been added. The solution so obtained is to be "examined" spectroscopically in as thick a layer as possible, and the absorption bands of oxyhæmoglobin looked for. If the two bands are visible then add two or three drops of ammonic sulphide, and in a few minutes the single band of reduced hæmoglobin will appear; shake this last solution for some time in the air, and the two bands will reappear.

(*b*) If the hæmoglobin bands cannot be found satisfactorily, try for the absorption bands of hæmatin. Mix the ammoniacal solution with glacial acetic acid till it is markedly acid, and transfer it to a small stoppered bottle; add its own volume of ether, and shake well for a short time. If the ether does not separate readily, add glacial acetic acid drop by drop until the precipitate that appears is deposited or redissolved. The ether then separates with a reddish brown color. This colored ethereal solution is next poured into a small glass vessel with parallel walls, and examined with the spectroscope; if not too dilute the acid hæmatin bands will be seen, particularly the sharply defined band in the red (over C) and a less intense band in the green.

(*c*) Treat a portion of the spot with a few c.c. of a cold saturated solution of borax at 40°, and examine spectroscopically. A somewhat similar spectrum may be obtained with cochineal solution, purpurin-sulphonic acid, etc.; but the cochineal is decolorized by chlorine water without yielding a precipitate; and the hæmoglobin, when reduced with sodic sulphide (1:5), gives the single band of reduced hæmoglobin.

(*d*) Dilute a portion of the solution with five to six volumes of water, and precipitate it with acetate of zinc solution (5 per cent.) Dissolve the washed precipitate in 1 to 2 c.c. glacial acetic acid, and examine spectroscopically for hæmatin, part of the precipitate also being tested as in D for hæmin crystals.

D. *By the Formation and Detection of Crystals of Hæmin.*—The blood spots or scrapings are treated with warm glacial acetic acid, and to the solution a few grains sodic chloride are added; heat over a spirit lamp for some time; fresh acid being added if necessary. It is advisable to repeat the addition of the acetic acid several times and to heat after each addition, and the formation of the crystals occasionally seems to be facilitated by moistening the residue after each evaporation of the acetic acid with a few drops of water, and evaporating this in turn before the next addition of acetic acid. Finally, the whole may be evaporated over a water bath.

The entire operation can be satisfactorily performed upon a glass slide (p. 211), and the preparation examined microscopically after the addition of a few more drops of acetic acid and the application of a cover glass. With a high power dark brown rhombic crystals, often arranged in stellate groups, make their appearance.

E. *In cases where the amount of blood is very small, not more than a drop or a stain,* proceed as follows, as the same specimen serves for each successive test (HOPPE SEYLER):—

1. Remove the spot or stain of blood.
2. Macerate it in a little water contained in a watch glass.
3. If no proper solution occurs, but merely a separation of the coloring substance, dry as completely as possible over sulphuric acid, so that a colored layer may be deposited.
4. Apply the spectroscopic test to this deposit.
5. Then try to produce hæmin crystals by adding a little sodic chloride and ten to twenty drops of glacial acetic acid, stirring well with a glass rod; when all is dissolved evaporate rapidly over a spirit lamp and complete the evaporation upon a water bath. When the odor of acetic acid is no longer perceptible examine with a high power. Instead of acetic acid alone a mixture of chloroform (6) and glacial acetic acid (1) may be used with advantage (SELMI).
6. Now wash the contents of the watch glass with a little water, and throw upon a small filter; hæmin is insoluble and will remain on the filter; treat it here with a few drops of caustic soda, when a greenish or red liquid will be obtained, according to the thickness of

the layer. Evaporate this to dryness in a porcelain crucible, calcine the residue, and dissolve the ash in a little pure hydrochloric acid; then evaporate the excess of acid, add a few drops of water, and test for iron by means of ferrocyanide of potassium and potassic sulphocyanide.

CHAPTER IX.

ESTIMATION OF SINGLE CONSTITUENTS OF BLOOD.

IN many of the following weighings it is best to allow the blood or serum to flow into a weighed capsule, and by a subsequent weighing of this, when covered, ascertain the increase of weight.

1. **Water and Ash.**—Twenty-five grams of serum, blood, or defibrinated blood are dried in a platinum crucible over a water bath, followed by a hot air bath at 110° to 120°. The loss in weight is due to the water, but the weighing should be repeated several times till a nearly uniform result has been obtained after repeated heatings. The crucible is next cautiously heated in a tilted position over a Bunsen lamp, and the temperature gradually increased until the ash is of a reddish white color. The heat must not be more than a feeble red heat; and it aids the combustion if after the water has been ascertained the dried mass is removed and finely powdered before being ignited.

2. **The Soluble and Insoluble Salts and Chlorides.**—(*a*) The ignited mass, after it has been weighed, is to be repeatedly digested with water and then filtered. The insoluble residue, after having been dried, is again ignited until the carbon is completely burned. The weight of the residue is equal to the weight of the insoluble salts.

(*b*) The filtrate contains the salts soluble in water. Evaporate it to dryness in a weighed platinum crucible, heat to a dull redness, and weigh: this gives the soluble salts.

(*c*) This last residue is dissolved again in water, acidified with nitric acid, and the chlorides precipitated with silver nitrate; the beaker containing the mixture is next to be covered with a small box or otherwise protected from the light. When the precipitate has completely settled, the supernatant liquid is tested with a drop or two of the silver nitrate to ascertain if the chlorides are entirely precipitated. If this is the case, collect the silver chloride on a filter whose proportion of ash is known, wash it here with water containing nitric acid and then with pure boiling water; next dry at 100°, and melt the separated precipitate in a porcelain crucible; now let it stand aside and cool; the filter is then cut into little pieces and placed inside the crucible cover, and when it has been carefully calcined add the ash to the silver chloride in the crucible. This is to be covered, gently heated, allowed to cool over sulphuric acid, and weighed.

Example.—Twenty-five grams defibrinated blood dried and carbonized. After the extraction of the soluble salts and the complete combustion of the carbon the ***insoluble salts*** weighed 0·022 gram.

The watery solution evaporated in a platinum capsule and heated to faint redness gave 0·173 gram residue = the soluble salts.

The solution of the residue in water, acidulated with nitric acid and precipitated by silver nitrate, gave the following:—

	Grams.
Porcelain crucible with silver chlorides and ash of filter .	24·476
" "	24·231
	0·245
Ash of filter	0·002
Silver chloride	0·243

$$\begin{aligned} Ag &= 108 \\ Cl &= \ \ 35{\cdot}5 \end{aligned}$$

$$143{\cdot}5 = 35{\cdot}5 \text{ Cl; therefore } \frac{35{\cdot}5 \times 0{\cdot}243}{143{\cdot}5} = 0{\cdot}060 \text{ Cl.}$$

Calculating the percentages in the blood from these results, we obtain—

	Gram.
Insoluble salts	0·086
Soluble salts	0·678
Total salts	0·764
Chlorine	0·235 (GORUP BESANEZ).

3. **Fibrin.**—Twenty to thirty c.c. of blood collected directly from a vein are well stirred for ten minutes or so with an ivory or whalebone spoon in a previously weighed caoutchouc-covered bottle, the spoon passing through a slit in the caoutchouc; weigh again; and after it has stood some time remove the cover and wash the resulting fibrin with a little dilute sodic chloride solution. The fibrin is then collected on a tared filter and washed with dilute sodic chloride solution and then with pure water; it is subsequently transferred to a dish and washed there successively with water, alcohol, and ether, and after being dried at 110° it is weighed between clipped watch glasses.

4. **Fats.**—Ten grams defibrinated blood or serum are dried over a water bath and then in a hot chamber at 120°; the mass is pulverized, and is next digested repeatedly with ether, and the ethereal solution evaporated. A yellow semisolid fat is left behind: weigh this; then treat with cold alcohol, when a crystalline fat will be removed and an oily fat left behind. This latter may be weighed after evaporating off the alcohol.

5. **Albumens, etc.** (*a*) *By Heat Coagulation.*—Five grams of blood or serum are diluted with 25 grams of water, then acidulated with dilute acetic acid and boiled. The coagulum is collected on a previously dried and weighed filter and well washed there with water, alcohol, and ether, dried at 110°, and weighed. The coagulation may be produced by boiling 20 grams of water in a large porcelain capsule, and then adding to this the diluted blood or serum; a little acetic acid is subsequently added, and the boiling continued until the albumen has separated completely.

If the liquid from which the coagulum has been separated, together with the washings of the latter, is evaporated to dryness over a water bath and then at 110° for some time, and weighed, we obtain the *extractives and salts.* Calcine completely, let cool, and weigh again; the loss in weight corresponds to the *extractives*, while the difference is the weight of the *soluble salts.*

(*b*) *By Alcoholic Precipitation.*—To 20 or 30 grams of the blood or serum neutralized with dilute acetic acid add 10 volumes absolute alcohol, lay aside for a few days; next collect the precipitate on a weighed filter, and after washing it with dilute spirit, absolute alcohol, ether, and hot and cold water in succession, dry it at 110°; now weigh it when it has been cooled over sulphuric acid. If accurate results are required the coagulum should be calcined and the weight of the ash obtained subtracted.

(*c*) The polariscope can also be employed in the determination (see under Urine, Book IV, Chapter XIX).

6. **The Corpuscles.**—(*a*) Defibrinated blood is mixed with three times its volume of saturated solution of sodic sulphate, laid aside for 24 hours, and then filtered. The corpuscles remaining on the filter are then plunged into boiling concentrated solution of sodic sulphate, and afterwards washed in distilled water, dried, and weighed. Instead of filtering we can decant, and after washing the deposit with the sodic sulphate by decantation we add to it four times its volume of alcohol, which renders it insoluble. After some time the the alcohol is decanted off, the deposit washed again, dried, and weighed: the the weight will be the hæmoglobin+the albuminoids of the corpuscles.

(*b*) Another plan for the estimation of the corpuscles is *by enumeration.* A known volume of blood is diluted 100 times or so with a neutral fluid; of this a minute quantity is taken, and the corpuscles in it counted.

1. MALASSEZ' *plan* is the following: The finger is pricked and the blood sucked up into a fine graduated capillary tube provided with a dilatation near its upper end; above and below the dilatation is a mark: by drawing the blood up as far as the lower mark, and then drawing up the artificial serum till the upper mark is reached, we have a mixture containing 1 per cent. of blood. The two fluids are mixed in the dilatation, which contains a small glass bead to facilitate the intermixture. A 10 per cent. solution of sodic sulphate may be used as the artificial serum, or a solution thus prepared: solution of gum Arabic (sp. gr. 1020) one part, and a solution of equal parts of sodic sulphate and sodium chloride having a sp. gr. of 1020 three parts. The blood thus diluted is next introduced into a graduated flattened capillary tube, and a portion of this is examined with a high power, the eye piece of the microscope being provided with a micrometer divided into square millimetres. The process of enumeration must next be proceeded with; and, knowing the length of the tubes covered by the squares, a little calculation will determine the corpuscles present in a cubic millimetre.

(2) HAYEM'S *method as modified by* Dr. GOWERS is effected with the following parts: a small pipette fitted with an elastic tube holding up to a mark on its stem 995 cubic mm., a capillary tube marked to contain 5 cubic mm., a glass mixing jar and stirrer, and a brass stage plate provided with a glass slide on which is a cell $\frac{1}{5}$ mm. deep and whose base is divided into $\frac{1}{10}$ mm. squares. The mixing fluid consists of a solution of sodic sulphate of about sp. gr. 1025; 995 c.mm. of this are placed in the mixing jar, and 5 c.mm. of blood fresh drawn from a puncture in the finger are transferred by means of the graduated capillary tube to the same. The fluids are well mixed, and a small drop is transferred to the centre of the cell on the glass slide. This is covered, and the slide placed on the stage of the microscope. The corpuscles soon sink; the number in ten squares is then counted, and this being multiplied by 10,000 gives the mumber of corpuscles in a c.mm. of blood.

The blood of the capillaries contains $5\frac{1}{2}$ millions in each c.mm. (cubic millimetre), and about 1 pale corpuscle to every 350 or 500 colored corpuscles—a proportion, however, which is greatly increased in certain diseases, and normally after food.

7. **Urea.**—100 grams defibrinated blood are placed on a dialyser that floats in about 100 c.c. to 20 c.c. of absolute alcohol. In a few hours the fluids of the blood holding the urea in solution will have dialysed out into the alcohol. The contents of the dialyser, which solidify after a time, are mixed with a little

water and the process repeated, so as to extract all the urea present. Some oxalic acid is then added to the alcohol, and this is evaporated to dryness on a porcelain dish. Crystals of oxylate of urea, with some fat, coloring matter, and sodium chloride, are present in the residue; and by treating the latter with petroleum naphtha the oxalate of urea is left behind, and it is to be dissolved in water, mixed with baric carbonate, and evaporated to dryness; or the urea can be extracted by ethyl acetate after the removal of the light petroleum (HAYCRAFT). If the latter plan is not adopted, then boil the dry residue with alcohol, and on evaporating the alcoholic solution pure crystals of urea are obtained, the amount of which can be determined by weighing, by decomposition with sodic hypobromite after the addition of a little sugar, or by Simpson's method (see Urea).

8. **Uric Acid.**—This determination is rarely required except in cases of gout or rheumatism. The serum (about 20 c.c.) is dried, and the residue rubbed up with hot alcohol. After standing some time the alcohol is decanted, and the residue digested with distilled water and then boiled, the watery solution being filtered and evaporated to a syrupy consistence. This syrupy fluid, if allowed to evaporate spontaneously, will soon show on its surface small white tufts of acicular crystals of urate of soda. A few drops of the solution will also give the murexid test (Book IV, Chapter VIII); or if acidulated with acetic acid and allowed to evaporate, crystals of uric acid will form in abundance.

A rapid modification of the same process is to place two drachms of the serum in a large watch glass, acidulate with acetic acid, and after inserting a linen thread in the fluid set it aside to evaporate, and uric acid crystals will soon be formed along the thread (GARROD).

9. **Sugar.**—(*a*) Dilute the serum with 5 times its volume of water, add dilute acetic acid, boil and filter. The concentrated filtrate is then tested for sugar with Fehling's solution (MERING).

(*b*) To separate the albumen more completely it will be found advantageous to put the serum into a small capsule, and having added to it an equal bulk of coarsely powdered sodic sulphate crystals, to boil for some time; then filter, wash the precipitate, and test the filtrate with Fehling's solution.

(*c*) Put the weighed blood into a mortar and rub it up with sufficient animal charcoal to form a dry paste; then mix it with a little water and filter, washing the mass on the filter thoroughly with water. The filtrate contains the sugar.

(*d*) Precipitate the blood with strong spirit and cover the coagulum with 4 times its volume of absolute alcohol; filter after 4 or 5 days; decant the spirit and distil it; extract the residue with more alcohol, and evaporate again. Now test a solution of the dry residue for sugar by the fermentation process.

(*e*) 40 grams sodic sulphate in small crystals are placed in a beaker, 20 c.c. blood added, and the beaker and its contents weighed. Stir the blood and crystals together, pour 30 c.c. of a hot concentrated solution of sodic sulphate over the mixture, and boil for some time. Remove the small coagulum, wash it thoroughly in more of the sodic sulphate solution, and add the washings to the contents of the beaker, which are then to be boiled and filtered. The filtrate is to be again rapidly boiled with excess of potassio-tartrate of copper (20 to 30 c.c. Fehling's solution). Now filter through glass wool, and the suboxide having been collected and washed with distilled water, dissolve it in a litttle nitric acid after the addition of a few drops of hydric peroxide. The dissolved copper has next to be electrolytically deposited on a platinum spiral, the galvanic action requiring to be steadily and continuously maintained for at least twenty-four hours. The increase in weight of the spiral, after it has been washed in water and spirit and subsequently dried over a water bath, multiplied by 0·5678 gives the amount of glucose (PAVY).

CHAPTER X.

PATHOLOGY OF THE BLOOD.

I. Types of Pathological Variations (GAUTIER).

1. In anæmia and chlorosis, and in all chronic maladies generally, as a consequence of hæmorrhages, we find the *corpuscles and fibrin diminished and the water increased.*

2. In the invasion of intermittents, in the decline of the exanthemata (variola, scarlatina, etc.), in the early stages of phthisis, in typhoid conditions, in Bright's disease, and in some cases of chlorosis, *the corpuscles are diminished, the fibrin normal or slightly increased, and the water increased.*

3. In plethora, in the invasion of the exanthemata, in the reaction period of intermittents, *the corpuscles are increased, the fibrin normal or slightly diminished, and the water diminished.* The water is also diminished in continued fever, diarrhœa, and cholera.

4. In the early period of inflammatory fevers, as pneumonia, pleurisy, erysipelas, and rheumatism, *the corpuscles are normal or diminished, the fibrin increased, and the water normal.* Later in these diseases the corpuscles fall below the normal.

5. When in the course of a chronic affection an inflammation is lighted up, as in the last stage of phthisis or in typhoid fever, then *the corpuscles are diminished and the water and fibrin increased.*

II. The Blood under Pathological Conditions (*after* GORUP BESANEZ).

(See table, p. 226.)

The *oxygen* of the blood increases in inflamed conditions, and we generally find a greater proportion than the normal both of oxygen and carbonic acid in the blood coming away from an inflamed organ or tissue.

In *septicæmia* the colored corpuscles are much altered, their specific gravity being lessened, and some loss occurring both in their salts and hæmoglobin. There is an increase in the pale corpuscles, the fats, urea, and carbonic acid, and an abundance of free granules, bacteria also at times making their appearance, as well as an occasional excess of lactic acid and ammonic carbonate; and a diminution in the amount of fibrin and albumen, the latter body also appearing to be altered in quality; further, less oxygen and glucose are said to be present.

In *chlorosis* the number of the colored corpuscles is lessened; their size likewise is said to diminish slightly, as also the proportion of iron and hæmoglobin present in them. In this disease, as well as in leukæmia, pyæmia, and puerperal fever, the pale corpuscles are greatly increased; and a similar increase may be noted in some cases of tubercle and pneumonia.

The proportion of *albumen* is increased in chyluria, intermittent fever, cholera, in the early stage of typhus, and after drastic purgatives, but diminished in most diseases in which the fibrin is increased, particularly where much exudation occurs.

The *fats* increase when the circulation is interfered with; also in pneumonia, chronic alcoholism, diabetes, and in some cases of acute and chronic poisoning.

Diseases.	Abnormal constituents.	Water.	Fibrin.	Corpuscles.	Albumen.	Extractives.	Urea.	Sugar.	Fats.	Salts.
Ac. exanthemata .	—	—	—	diminished.	—	—	—	—	—	increased.
Arthritis	uric acid	occasionally diminished.	—	—	—	—	increased.			
Bright's disease .	uric acid occasionally	—	increased.	diminished.	diminished.	—	increased occasionally 1·5 per cent. in the serum	—	increased.	increased.
Chlorosis	—	increased.	increased.	diminished.						
Cancer	—	—	increased.							
Cholera	ammonic carbonate .	diminished.	—	increased.	increased.	—	increased.	—	increased.	diminished.
Chyluria	—	—	—	—	—	—	—	—	increased.	
Cretinism . . .	—	increased.	diminished.	diminished.	diminished.					
Diabetes	—	increased.	—	—	—	—	—	increased may be above 0·9 per cent.		
Dysentery . . .	—	—	increased.	diminished.	diminished.	—	—	—	—	increased.
Inflammations and inflammatory fever.	—	increased in early stage.	increased.	diminished.	diminished.	—	increased.	—	increased.	slightly diminished.
Intermittent fever	—	—	—	—	increased.	—	—	—	—	increased.
Jaundice and suppression of bile.	bile pigments and biliary acids.	—	—	—	—	—	—	—	increased.	
Leukæmia . . .	pseudogelatin; formic, acetic, lactic, and uric acids; xanthin, hypoxanthin, leucin, and glycogen (?)	—	—	pale corpuscles increased.						
Liver diseases . .	tyrosin and leucin .	—	—	—	—	—	—	—	increased.	
Malaria	bile pigments . . .	—	diminished.	increased.	diminished.	—	—	—	diminished.	
Plethora	—	—	—	increased.	increased.					
Puerperal fever .	bile pigment and free lactic acid.	diminished.	increased.	diminished.	diminished.	increased.				
Pyæmia	—	—	diminished.	pale corpuscles increased.						
Scurvy	—	increased.	increased.	diminished.	—	—	—	—	—	diminished.
Typhus:—										
Early stage . .	—	diminished.	increased.	increased.	increased.					
Later " . .	—	increased.	—	diminished.	diminished.	increased.	—	—	—	increased.
Uremia	ammonic carbonate (?)	--	—	—	—	—	increased.			
Yellow fever . .	—	—	—	—	—	—	increased.			

While normal blood furnishes from 0·1 to 0·4 per cent. of dry *fibrin*, the proportion has been found as high as 1 to 1·2 per cent. in acute erysipelas, and from 0·5 to 1 per cent. in acute pneumonia. An increase occurs in the early stages of typhus, dysentery, puerperal fever, chlorosis, scurvy, and Bright's disease; in hydræmia it is diminished.

Leucin and tyrosin make their appearance in the blood in most cases of yellow atrophy of the liver.

III. Alterations produced by Certain Toxic and other Agents, Hæmorrhage, etc.

The proportion of *sugar* is frequently increased after poisoning with chloroform, chloral, curara, nitro-benzol, and amyl nitrite.

In *lead poisoning* the corpuscles are diminished in number, but their individual volume is said to be increased.

Antimonial compounds act rapidly on the blood, increasing its fat and cholesterin, and apparently diminishing its gases, and giving it an anæmic character. Under the use of *arsenic* the fat and cholesterin increase; and in cases of antimonial as well as arsenical poisonings the biliary acids have been noticed to be increased.

Under the influence of *phosphorus* the fat, cholesterin, and fibrin increase, the albumen diminishes, and the corpuscles are altered, the hæmoglobin occasionally appearing to become crystalline in their interior.

Quinine and alcohol are said to increase the volume of the corpuscles, while morphine and carbonic acid produce the inverse effect (MANASSEÏN).

Bile or the biliary acids injected into the vessels cause a crystallization of the hæmoglobin, the corpuscles undergoing much alteration, the blood being rendered anæmic and its fat and cholesterin increased. In many cases of jaundice it is possible that somewhat similar results are gradually induced.

Sulphuretted hydrogen renders the blood brown and then greenish in tint; *carbonic oxide* gives it a cherry red, *chlorine gas* a greenish yellow, and arseniuretted hydrogen a brownish ochre coloration—phosphuretted and antimonetted hydrogen having a similar but weaker action than this last gas. Under the influence of *nitrous oxide* there is a tendency to a displacement of the oxygen of the corpuscles, the exhalation of the carbonic acid at the same time being diminished; the blood has at first a dark tint, but it afterwards assumes a bright red color; there is further an increased excretion of water, urea, and uric acid by the kidneys.

In animals poisoned by *nitrites*, as nitrite of amyl, the blood is of a chocolate color, with abundance of methæmoglobin (HOPPE SEYLER).

As the *result of hæmorrhages* the corpuscles diminish in number, but the fibrin appears to increase (DELAFOND), although some maintain the contrary. Bleeding increases the water and lessens the oxygen, but it affects slightly or not at all the proportion of albumen and salts. The blood, however, rapidly recovers its normal condition.

In dogs that were allowed to eat freely after blood-letting it was found that while the proportions of the inorganic constituents of the serum remained constant the organic solids diminished suddenly and continued to diminish for several hours; after which time they began to increase, and continued to do so till, after 14 days, they exceeded the normal quantity. When, on the other hand, the dog was kept without food, it was found that the solid substances of the serum, which had diminished immediately after the blood-letting, began to increase sooner than in the former case, so as to exceed the normal amount after two days. In this experiment it was noticed that when food was given to the animal the proportion of solids in the serum immediately diminished.

Different organisms are occasionally to be met with in pathological blood. In tuberculosis, for example, bacilli are present in great numbers, and appear to be the cause of the disease. They may be detected in the serum by a mixture of alkaline methylene blue and vesuvine, whereby they alone are colored blue (KOCH, BAUMGARTEN, TOUSSAINT).

CHAPTER XI.

LYMPH AND CHYLE.

THE lymph carries into the blood the products of the functional activity of the lymphatic glands, as well as of the retrogressive metamorphosis of the different tissues of the body. While the chyle is the assimilable extract of the chyme, the lymph may be regarded in great part as the overflow of the interstitial fluid which is constantly being renewed and modified by the blood.

While an animal is fasting its chyle is clear and transparent, and the same can be said for the lymph in the thoracic duct; indeed, the contents of the lacteals and lymphatics may be said to be identical until after a meal, when the fluid in the lacteals and in the duct becomes milky in appearance, owing to its being charged with fatty particles.

I. **LYMPH. Amount.**—It is very difficult to form a correct estimate of the total amount of lymph and of the interstitial fluids of the body. All the constituent parts of the tissues and organs are, we know, bathed, as it were, in an interstitial fluid, which, together with the contents of the lymphatic vessels in direct continuity with the interstitial spaces containing this fluid, has been estimated as high as one-third to one-fourth the weight of the body.

Of chyle and lymph it is reckoned that for every 220 lbs. of body weight about 13½ lbs.—that is, a quantity of fluid equal to the whole blood—pass through the thoracic duct in the twenty-four hours, about 7½ lbs. being chyle from the intestine and 6 lbs. lymph from the tissues (SCHMIDT).

Physical Properties.—Lymph is a transparent, whitish, opalescent, or even yellowish or faintly reddish, slightly viscid fluid, that is less alkaline than blood, and having a density of 1022 to 1037, or occasionally as high as 1045 (KRIMER). When removed from the body, lymph coagulates in five to twenty minutes. It consists of plasma and corpuscles. The latter are identical with the pale corpuscles of the blood, and are chiefly derived from the lymphatic glands, from which the lymph is constantly carrying these bodies in great numbers into the blood. At certain points of its course the lymph also contains small fatty granules like those of chyle, and colored corpuscles are occasionally met with.

Chemical Composition.—Lymph is very variable in composition. It may be stated generally to be—

Water	93 to 98	per cent.
Solids	6 " 2	"
Albumen	3·2 to 0·3	"
Fats	2·5 } " 0·15	"
Extractives	0·1 }	
Ash	0·7 " 0·8	"

The solids average about 4 to 4·6 per cent., and the sodic chloride about 0·6 per cent. (NASSE).

Human Lymph, etc.

	(SCHMIDT.)	(GUBLER and QUEVENNE.)	(HENSEN and DÄHNHARDT.)
Water	96·39	93·48	98·52
Solids	3·6	6·52	1·48
Fibrin	—	0·6	
Globulin substances and serum albumen	2·9	4·28	0·68
Fats, cholesterin, lecithin		0·91	
Extractives		0·43	
Sugar		0·05	
Salts	—	0·82	0·79
Sodic chloride	0·54		
Soda	0·15		

Ash of Human Lymph (DÄHNHARDT, in 100 parts of Ash).

Sodic chloride	74·84
Soda	10·35
Potash	3·22
Lime	0·93
Magnesia	0·26
Phosphoric acid	1·09
Carbonic "	8·21
Sulphuric "	1·27
Ferric chloride	0·06

The sodic chloride, it may be seen, is specially abundant, and the phosphates very scanty.

SCHMIDT gives the following analysis of the lymph of a cow:—

Serum	95·52
Clot	4·42

	In 100 parts serum.	In 100 parts clot.
Water	95·76	90·73
Fibrin	—	4·86
Other albumens	3·20	
Fats	0·12	3·43
Organic matter	0·17	
Salts	0·74	0·96
Sodic chloride	0·56	0·60
Soda	0·13	0·06
Potash	0·01	0·10
Sulphuric and phosphoric acids and earthy phosphates	0·04	0·23

The lymph cells contain an excess of potash and phosphoric acid as compared with the serum, the latter having an excess of soda. The serum also contains in suspension a few fatty granules and some pale corpuscles; about 2 to 3 per cent. or even more, of albumens coagulable by heat, and 0·2 to 0·3 per cent. of proteids not coagulable by heat, but precipitable by alcohol;

further, it contains more urea than is present in chyle (about 0·019 per cent. in the cow), and grape sugar is always present (about 0·16 per cent. in the dog).

Gases in 100 Volumes of Lymph at 0° and 760 mm. (HAMMARSTEN).

Oxygen	0·0	to	0·10
Nitrogen	1·12	"	1·82
Carbonic acid	37·5	"	47·13

The carbonic acid gas is more abundant than in arterial, but less so than in venous blood, the tension in venous blood equalling 3·9 and that in lymph 3·47 per cent.

II. **CHYLE.**—This fluid is the assimilated extract of the chyme, being absorbed from the digested food by the intestinal villi, and forming the material from which the blood is constantly renewed.

Physical Properties.—It forms a milky white, or occasionally a yellowish or reddish opaque fluid, having an alkaline reaction, a faint smell, a saltish taste, and a specific gravity varying between 1007 and 1022.

In its passage from the intestine into the *receptaculum chyli* the chyle undergoes important modifications. At first it contains albumen in solution, and oily matter in a state of fine subdivision—the *molecular base*—and is uncoagulable; but as it passes onwards and has traversed a lymphatic gland, corpuscles (about $\frac{1}{4000}$ inch in diameter) begin to show themselves; these afterwards increase in size ($\frac{1}{2500}$ to $\frac{1}{3000}$) and acquire a more distinctly cellular character, the fine granulations at the same time diminishing greatly in number; and the fluid becomes coagulable from the presence of fibrin. Large granulations are also met with, probably *débris* of the corpuscles, and also colored corpuscles in the way of development. The chyle therefore becomes impoverished in solids, and particularly in albumen and fatty matters, in its onward progress, and enriched in corpuscles and fibrin.

Chemical Composition.—The composition of the chyle is very variable not only in different animals but also in the same animal at different times. It is made up of formed elements that float in a plasma. Of the former there are pale corpuscles identical with those of lymph; a few colored corpuscles, especially in the thoracic duct; also the molecular base, consisting of finely granular fatty particles.

The plasma generally coagulates pretty rapidly, and gives a fibrin clot and serum. Fibrin is absent before the chyle has passed through the lymphatic glands. The clot becomes pink in the air, owing to the presence of immature colored corpuscles.

The serum contains, dissolved in water, the following constituents:—

(*a*) Globulin, alkali albuminate, serum albumen, and peptones in small amount, rising during digestion to 0·6 to 0·7 per cent.

(*b*) Cholesterin, lecithin, and fatty soaps.

(*c*) Grape sugar, varying in amount from mere traces to as high as 2 per cent.; and a diastatic ferment in traces.

(*d*) Urea (probably a constituent of the intermixed lymph) and alkaline lactates (especially in the herbivora and after starchy food).

(*e*) Inorganic salts of the alkalies and alkaline earths, iron, phosphoric acid, etc.

Analysis.

	Human Chyle (O. Rees). Per cent.	*Chyle of Dog* (Hoppe Seyler). Per cent.
Water	90·48	90·67
Solids	9·52	9·02
Fibrin	a trace	0·11
Albumen	7·08	2·10
Fats, lecithin, cholesterin, etc.	0·92	6·48
Extractives	1·0	Fatty acids, soaps, etc. 0·23
Salts	0·44	0·79

In the *ether extract of chyle*, obtained from a human fistula, the following bodies were present in the 100 parts:—

Cholesterin	11·3	to	14·1
Lecithin	7·5	"	8·8
Olein	38·1	"	77·1
Palmitin and stearin	43.0		

Chyle of Horse (C. Schmidt).

Serum	96·74
Clot	3·25

Water	95·85	88·7
Solids	4·15	11·2
Fats	0·05	0·15
Soaps	0·03	0·03
Fibrin	—	3·89
Albumen, sugar and extractives	3·08	6·59
Hæmatin	—	0·20
Sodium chloride	0·59	0·23
Soda	0·11	0·13
Potash	0·01	0·07
Phosphates and sulphates, etc.	0·03	0·11

The mineral salts of chyle, which appear to be the same as those of liquor sanguinis, vary from 0·7 to 1·4 per cent., and of these the chief are salts of the alkalies. A diastatic ferment is also stated to be present (Grohé), and the sugar is said sometimes to amount to as much as 2 per cent. (Colin). When the animal has been fed on a purely fatty diet, as much as 14·6 per cent. of fat has been found in the contents of the thoracic duct (Zawilski). In a fasting animal the chyle is poorer in water and richer in solids, particularly corpuscles, fibrin, and albuminoids, than during digestion.

Methods.—1. Kill a rabbit that has been well fed some three or four hours previously, and having opened its abdomen and drawn out a portion of the small intestine, try to collect a little chyle by plunging a capillary glass tube into the intestinal wall.

2. Examine a drop of this on a slide, and observe the pale corpuscles, which so closely resemble, and in fact are identical with, those of the blood, and which lie in the midst of a mass of fine granules, mainly fatty in their nature—the so-called *molecular basis.*

3. Now irrigate with ether and note that the granules do not disappear, but that they will do so if (4) a drop of caustic potash or acetic acid has been previously added, showing that the particles are invested by an albuminous coating that keeps them from coalescing.

5. The rest of the chyle in the capillary tube should be examined from time to time under a low magnifying power, and it will soon be seen to coagulate, white threads of fibrin separating, as in the coagulation of liquor sanguinis.

CHAPTER XII.

SEROSITIES AND TRANSUDATIONS.

In health the amount of serosity is very slight. It is generally clear with a yellowish tint and an alkaline reaction, and is coagulable by heat; it contains many of the blood constituents, and among others one or more of the fibrin generators, fibrinogen, being the more common. Some of the fresh transudations coagulate rapidly spontaneously, while others require the addition of ferment and paraglobulin, and others again furnish no coagulum. Normal transudations are quite transparent, but those occurring in pathological conditions are often opaque, occasionally milk white or brown, and frequently contain pus or epithelial cells, fat granules, cholesterin plates, and altered blood. Normal transudations are poorer in solids, and particularly in albuminoids, than blood serum.

1. **Physiological Transudations.**—*Human amniotic fluid* is a yellow or brownish, often turbid, weakly alkaline or neutral fluid, having a very variable specific gravity (1002 to 1028). After the eighth or ninth week the secretion of the fœtal kidneys is mixed with it. Among the constituents of the amniotic fluid we find mucin, globulin, a vitellin-like body, and urea; lactic acid, kreatinin, grape sugar, alkaline carbonates, and free carbonic acid have also been found in this fluid in some animals. The sediment consists of mucus corpuscles and epithelial cells. In the early months it is richer in solids, particularly albumen, than it is at a later period.

Cerebro-spinal fluid is clear and strongly alkaline; its proportion of solids is small (1·1 to 1·9 per cent.), and it is particularly poor in organic constituents. Potash salts are more abundant in this fluid than soda salts, though sodic chloride may sometimes be the chief inorganic constituent and constitute half the total ash, the potassic phosphate only forming about a third. A body is also present resembling sugar, except in being devoid of polarizing action on light. In fractures of the base of the skull this fluid sometimes exudes by the ear.

The pericardial fluid generally contains fibrinogen and fibrinoplastin, and accordingly, like blood, may coagulate spontaneously, but fibrinoplastin may be absent. It is the richest in fibrinogen of all the normal serous fluids, and contains about 4·5 per cent. solids, of which 0·7 per cent. is inorganic and 3·8 per cent. organic, 2·5 per cent. being albuminous in its nature. The amount of this albumen falls in cirrhosis of the liver, but rises in Bright's disease.

The aqueous humor is clear and transparent, weakly alkaline, and has a specific gravity of 1003 to 1009, and contains about 0·7 per cent. of sodium chloride and 0·05 per cent. of potassic phosphate.

The synovia is the liquid secreted by the synovial membrane of joints. It is closely allied to mucus, and in its formation a somewhat similar process possibly occurs. Synovia is a clear, yellowish, more or less viscid and thready, alkaline liquid, containing much mucin; it is especially rich in solids, consisting of albumen, fatty granulations, and salts, especially sodium chloride and traces of alkaline carbonates and sulphates; its composition, however, is not constant, and it is affected by the condition of the joint as to rest or activity: with much exertion, attended with increased movement of the joint, for example, the synovia diminishes in quantity, becoming more viscid, its albumen and mucin augmenting and its water and salts decreasing.

	From the joint of an ox at rest (stall-fed).	From the joint of a grazing ox.
Water	96·9	94·8
Solids	3·1	5·2
Mucin	0·24	0·56
Albumen and extractives	1·57	3·51
Fats	0·06	0·07
Salts	1·13	0·99

II. Morbid or Pathological Serosities or Transudations.—These are produced at the free surface of serous membranes. In the normal state a serous membrane is simply moist, but in many diseases a copious exudation occurs.

The *character of the liquid* differs considerably, according to the *seat* of its production and to the *presence or absence of inflammation*, in the latter case the exudation not being so rich in albumen, salts, fatty matters, and extractives. The *age* of an exudation considerably affects its solids, as the water may be absorbed, and accordingly a greater density produced; the same may also take place if much fluid is lost in any way by the system at large, as after profuse diarrhœa or sweating. Less albumen also is likely to be present if there is any continuous loss of this body, in consequence of hæmorrhages, or in Bright's disease.

The ordinary constituents of a transudation are water, serum albumen, fibrinogen, fats, soaps, cholesterin, and inorganic salts; also carbonic acid gas and traces of oxygen and nitrogen.

Fluid of anasarca is clear and watery, occasionally slightly yellowish in tint, having an alkaline reaction and a specific gravity of 1005 to 1010. It contains serum albumen about 0·5 per cent.; urea, 0·1 to 0·2 per cent.; and, if fresh, grape sugar 0·03 to 0·08 per cent.; of carbonic acid gas there is present about 17 per cent. loosely and 7 to 24 per cent. closely combined, together with traces of oxygen and nitrogen.

Ascitic fluid has a specific gravity of 1008 to 1012; the inorganic constituents amount to 0·7 to 0·9 per cent., while the organic vary very much. The color is generally yellow and the reaction alkaline. After frequent tappings the solids diminish in quantity; an increase in the solids, however, is a favorable sign (MÉHU). A poverty in the saline constituents may also be looked on as a sign of imperfect nutrition. The proportion of fibrinogen is less than in a pleural effusion. Among its organic elements are found urea, uric acid, kreatin, xanthin, and cholesterin. It contains about 10 per cent. of carbonic acid gas, about 37 per cent. of which is loosely combined; there are also traces of nitrogen and oxygen. The ascitic fluid from a case of tubercular peritonitis may show a milky layer on its surface after standing. In some forms of ascites also fatty granules are suspended in the fluid, and in cancer of the liver a precipitate may be given with basic lead acetate which becomes blue on standing.

Pleuritic fluid.—The normal secretion is too small to admit of analysis; in abnormal effusions, however, it is abundant, having a specific gravity of 1005 to 1020, or if any pus is present the density may be as high as 1029. The reaction is alkaline unless the fluid is very purulent, when it may even be weakly acid. The solids generally amount to 5 to 7 per cent. The carbonic acid gas varies between 40 and 60 per cent., but the presence of pus diminishes this proportion greatly, for with a purely purulent effusion it may fall to 8 per cent.; only mere traces of nitrogen and oxygen show themselves.

The fluid of *ovarian cysts* contains paralbumin and mucin, as well as different colloids and peptones; it is often of a glairy consistence. The fluid of *strumous cysts* is generally brownish red, thin, and strongly alkaline; it frequently clots on cooling, and contains a body like paralbumin. In *echinococcus cysts* the fluid is mostly colorless, neutral, and weakly opalescent, containing 1·4 to 2 per cent. of solids, and having a specific gravity of 1006 to 1015. The amount of albumen is insignificant; sugar is often present in about ½ per cent., inosit in about 1 per cent., together with traces of urea, kreatin, and succinic acid.

The hydrocele fluid, according to MÉHU, is very rich in solids—even more so than blood serum; fibrinogen is abundant, and fibrinoplastin is not always wanting, although it is never present except in very slight amount, and only in a small proportion of cases.

In the *fluid of intestinal fluxes* the potash salts generally exceed those of soda, and a considerable amount of phosphoric acid is present; sometimes also albumen, much mucus, and blood.

Reference has already been made to the *gases of these different transudations*, which usually contain from 40 to 60 per cent. carbonic acid gas, exhibiting a high degree of tension; 1 to 2 per cent. nitrogen, and 0·1 to 0·6 per cent. oxygen. Pleuritic effusion and fluid of hydrothorax contain from 4 to 84 per cent. carbonic acid gas; hydrocele fluid, about 65 per cent.; dropsical fluid of the extremities, 31 per cent.; peritoneal fluid, about 14 per cent. Of oxygen and nitrogen proportions varying from ¼ to 2 per cent. have been obtained, the nitrogen being more abundant than the oxygen (EWALD and PLANER).

I. *Transudations in a Case of Albuminuria* (SCHMIDT).

	Pleura.	Peritoneum.	Cerebral ventricles.	Areolar tissue of extremities.
Water . . .	96·39	97·89	98·35	98·87
Solids . . .	3·60	2·10	1·64	1·13
Organic .	2·85	1·13	0·79	0·36
Inorganic .	0·75	0·97	0·84	0·77

II. ***Table of Analyses of Different Serous Transudations** (**chiefly Human**) **compared with Blood Serum*** (altered from Gorup Besanez).

Constituents in 100 parts.	Blood plasma (Schmidt).	Blood serum.	Serum of pus.	Cerebro-spinal fluid (Schtscherbakoff).	Fluid of spina bifida.	Amniotic fluid (Prochownik).	Allantoic fluid (Majewski)—cow.	Aqueous humor of eye of calf (Lohmeyer).	Vitreous humor of eye (Lohmeyer).	Tears (Lerch).	Fluid of blister.	Ascitic Fluid (Vogel).	Pericardial fluid (Gorup Besanez).	Acute pleuritic effusion (Méhu).	Chronic pleuritic effusion (Méhu).	Hydrocele (Hammarsten).	Acute hydrocephalus (Schmidt).	Chronic hydrocephalus (Hilger).	Intestinal flux after purgation (Schmidt).	Dysenteric flux (Schmidt).	Echinococcus cyst.
Water	90·15	91·33	91·37	98·99	98·99	98·14	98·85	98·69	98·64	98·20	93·21	94·60	95·51	93·13	93·50	93·88	98·68	98·77	96·97	95·86	98·58
Solids	9·85	8·67	8·63	1·01	1·01	1·86	1·34	1·31	1·36	1·80	6·79	5·40	4·49	6·87	6·50	6·15	1·32	1·23	3·03	4·14	1·41
Fibrin	0·80	—	7·72	—	—	—	—	—	0·02	—	4·92	—	0·08	0·81	—	0·59					
Albumen	8·19	7·25		0·18	0·04	0·52	—	0·12	0·13	0·50		3·30	2·47	0·08	6·06	4·94	0·37	0·25	0·16	1·50	trace
Extractives . . .		0·64	0·93	—	0·14	0·77	1·24	0·42	0·32	—	1·05	0·13	1·27	5·50		0·40		—	2·01	1·46	0·60
Salts	0·86	0·78	0·77	0·81	0·81	0·56	0·80	0·07	0·88	1·32	0·76	0·80	0·67	0·81	0·86	0·92	0·95	0·76	0·86	1·18	0·83
Potassic chloride .	0·36	—	—	—	—	0·52	—	0·01	0·06	—	—	—	—	—	—	—	0·22	0·08	0·26		
Sodic chloride . .	0·55	—	—	0·54	—		—	0·69	0·77	0·30	—	—	—	—	—	0·61	0·44	0·40	0·20		
Potassic sulphate .	0·028	—	—	—	—		0·09	0·02	0·01	—	—	—	—	—	—	—	—	0·03	0·06		
Sodic phosphate . .	0·027	—	—	—	—		0·03	—	—	—	—	—	—	—	—	—	0·06	—	0·06		
Earthy phosphate .	0·052	—	—	—	—	0·04	—	0·04	0·02	—	—	—	—	—	—	—	0·03	0·09	0·05		

Compared with the blood serum it will be seen that the fluids of these transudations are richer in water, poorer in albumen, still poorer in fibrin generators, but relatively richer in crystalline constituents. The pleural transudation is richest in albumen and solids; then follow the peritoneal, cerebro-spinal, and subcutaneous œdematous effusions.

CHAPTER XIII.

PUS AND MUCUS.

I. **PUS** is a creamy, opaque, yellowish white or greenish gray fluid, produced as one of the consequences of inflammation. It is made up of corpuscles floating in a serous fluid. The corpuscles resemble, if they are not identical with, the pale corpuscles of the blood; they appear to be derived chiefly from the blood by a morbid migration of its pale corpuscles, although it is also very probable that some of them are derived from a later proliferation of the connective tissue or other corpuscles in the inflamed tissue. Frequently also we find granulation corpuscles, free molecules, molecular débris, and fatty particles. Its reaction is neutral or very slightly alkaline, this depending on the presence of alkaline carbonates and basic phosphates; and it has a mean density of 1032. The serum closely resembles that of blood, and, like it, contains serum albumen, fibrinoplastic material, a casein-like body, and another body like myosin; lecithin, cholesterin, fatty acids, and probably also xanthin and leucin are likewise present, particularly in altered pus, together with about eight per cent. loosely combined carbonic anhydride and a little hydrogen and nitrogen. In septicæmia the carbonic anhydride and hydrogen increase considerably, serous pus being especially rich in these gases.

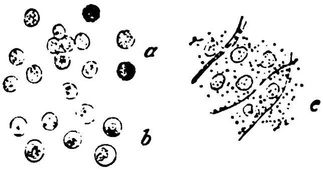


FIG. 22.—PUS AND MUCUS CORPUSCLES.

a, in a neutral liquid; *b*, after the action of dilute acetic acid; *c*, mucus from urine.

The proportion of corpuscles and serum is variable: fresh pus of most large abscesses contains 17 to 29 per cent. of corpuscles; the pus of some inflammations (meningitis, iritis, etc.) may be made up almost entirely of corpuscles; while, on the other hand, the pus coming from inflamed bones may only contain 2·5 to 3 per cent. of these bodies.

To separate the corpuscles, dilute the pus with a solution of sodic sulphate (1 part saturated solution to 9 parts of water) or of baric nitrate (1 part pus, 5 water, 5 concentrated solution of baric nitrate). After some hours the corpuscles can be obtained by decantation and then washed with more of the same fluid.

The *serum*, though containing in great part the same components, differs very considerably from blood plasma. They may be classified into albuminoids, as serum albumen, serum casein, nuclein, etc.; fats, as oleates, palmitates, and oleo-phosphoric acid; extractives, and a group consisting of protagon, lecithin, and cholesterin: also inorganic salts, as sodium chloride, calcic phosphate, carbonate and sulphate, and earthy phosphates; and gases, chiefly carbonic acid. In some kinds of pus chondrin, mucin, glutin, etc., have been met with.

Pus generally gives a mean dry residue of 12·7 per cent., but this is very variable.

I. *Analysis of Pus from Abscess of Cheek.*

	Per cent.
Water	76·9
Solids	23·1
Albumen and dried corpuscles	18·0
Fat and cholesterin	2·4
Extractives	1·9
Alkaline and earthy salts	0·9

II. *Mean of Three Analyses of Pus* (T. C. CHARLES).

Water	88·27
Solids	11·73
Albumens	8·02
Watery extracts	1·39
Alcoholic “	0·38
Leucin, tyrosin, and certain extractives	0·08
Cholesterin	0·34
Lecithin, cerebrin, etc.	0·38
Fats	0·06
Inorganic salts	1·08
Sodic chloride	0·65
Potassic phosphate	0·19
Sodic “	0·09
“ carbonate	0·06
Calcic phosphate	0·06
Sodic sulphate	0·03

III. *Dried Pus Corpuscles* (HOPPE SEYLER).

	Per cent.	
Albumen	13·43	
Nuclein	33·45	
Lecithin	7·04	
Fats	7·01	
Cerebrin	5·08	
Extractives	4·33	
Insoluble bodies	20·07	
Organic		97·63
Sodium chloride	0·14	
“ phosphate	0·61	
Potassic “	1·20	
Earthy and iron phosphates	0·42	
Inorganic		2·37

IV. *Ash of Pus* (MIESCHER).

	Per cent.
Serum contains about	0·75
Dry corpuscles contain about	2·8

Ash of Corpuscles.

	Per cent.
Potassic phosphate	1·2
Sodic “	0·6
Phosphoric acid in organic combination	0·5
Earthy phosphates	0·4
Sodic chloride	0·1
	2·8

The pus will therefore be seen to resemble lymph closely; where, however, pus has lain long in an abscess we may meet with peptones, leucin, and tyrosin.

To analyse pus add to it a dilute solution of sodic sulphate, and after some time the corpuscles will settle, when the serum can be decanted. Boil a little of the serum, and a coagulum of serum albumen will be obtained; filter, dilute the filtrate with much water, and add a little acetic acid: a myosin-like body is precipitated. Filter again, and test for gelatin and chondrin, which are occasionally present, adding to one part a strong solution of mercuric chloride, which precipitates gelatin, and to the other part a strong solution of alum, which precipitates chondrin.

To test for the cholesterin, lecithin, fatty and albuminous materials contained in the corpuscles, consult the directions given under these different bodies, or follow the table given on p. 241.

The *pus corpuscles* are protoplasmic in their nature, and, as their composition is, or at least is supposed to be, identical with that of the pale corpuscles, the opportunity may here be taken of studying their protoplasm, which may be regarded as a type of animal protoplasm in general.

Protoplasm of Pus Corpuscles. (*a*) *Organic Constituents.* 1. *Albumens.*—There are at least five forms, of which three are soluble in water—an alkali albuminate, an albumen spontaneously coagulable at 48° or 49°, and a body like serum albumen, coagulating at 70°—and two insoluble in water, of which one is an albumen insoluble in sodic chloride solution, and dissolved with difficulty by dilute hydrochloric acid of $\frac{1}{10}$ per cent., and the other a hyalin substance (ROVIDA) of the nature of fibrin and allied to globulin, which is soluble in hydrochloric acid $\frac{1}{10}$ per cent. and in 1 per cent. soda solution (this forms the chief mass of the protoplasm of the pus corpuscle).

2. In addition to these albumens there are also lecithin, cerebrin, cholesterin, fatty soaps, and certain badly known extractives; in the living and yet amœboid cell glycogen is found.

Gelatin, chondrin, and paraglobulin are not present; nor in the fresh pus do we find free fatty acids, leucin, or tyrosin.

(*b*) *Inorganic Constituents.*—Salts of potassium, sodium, calcium, magnesium, and iron; part of the sodium is in the form of chloride, and the rest of the sodium, together with the remaining bases, are probably present as phosphates.

The *nuclei* of the pus corpuscles contain, besides lecithin and traces of ash, a body called *nuclein*, that forms their chief component. A soluble and an insoluble modification of this body are described. This body has also been described as present in spermatozoa, hepatic cells, and nuclei of blood corpuscles.

Nuclein, $C_{29}H_{49}N_9P_3O_{22}$. *Preparation.*—Treat pus corpuscles several times with warm alcohol to separate the fats and lecithin; then digest the residue with artificial gastric juice at 37 to 40°. After 24 hours collect the separated nuclei, which will be found in the bottom of the vessel, in a small loose filter, and wash them there with ether and then with cold water until the washings give no albumen reaction with tannic acid. Now extract the washed nuclei two or three times with warm alcohol. The purified mass is lastly extracted with very dilute caustic soda, the solution filtered and precipitated with hydrochloric acid, and the solution and precipitation again repeated. The precipitate, when well washed with boiling alcohol, is *soluble nuclein*, having the composition—

	Per cent.		Per cent.
C . . .	49·6	P . . .	2·5
H . . .	7·0	S . . .	1·8
N . . .	14·0	O . . .	25·1

The residue, insoluble in the dilute caustic soda, and which forms the greater part of the nucleus, is the *insoluble modification of nuclein*. It is soluble, however, in moderately strong solutions of the caustic alkalies and in strong hydrochloric acid; treatment with the latter, indeed, changes it into the soluble form.

Nuclein is colorless and amorphous, slightly soluble in water, but readily soluble in the alkalies and alkaline carbonates. Chloride of zinc, sulphate of copper, and nitrate of silver precipitate its solutions. Some chemists, it should be said, consider this body to be a mixture of one or more organic phosphorus-holding combinations with albumen.

Abnormal Constituents.—The body named *pyin* is really a mixture of albumens and not a chemical individual. It can be *obtained* by digesting recent pus with sodic chloride solution (10 per cent.) and filtering after 24 hours. The insoluble residue is treated with dilute hydrochloric acid and then filtered, the filtrate next treated with soda, and the precipitate collected and dried.

The so-called *pyocyanin* (FORDOS) is no normal constituent of pus, but is due to the presence of special blue-colored vibriones. A blue color is occasionally seen upon the bandages of suppurating wounds; it can be extracted from these by macerating the colored pieces in weak alcohol, then evaporating the alcohol, filtering hot, and shaking up the filtrate with a little chloroform; the chloroform is next decanted and treated with dilute sulphuric acid, when a red pigment passes into solution in the acid, while a yellow pigment (pyoxanthose) remains in the chloroform. The acid extract is saturated with baric hydrate, and the filtrate again shaken up with chloroform. On allowing a drop of the latter to evaporate on a slide fine blue needles will be seen under the microscope.

In jaundice the pus may contain bile pigments, and in diabetes sugar. Formic, butyric, and valerianic acids have likewise been met with.

II. **MUCUS** is the term given to the secretion of certain mucous membranes, which are generally provided with so-called mucous glands, but which in certain cases, as in the frontal and maxillary sinuses, the tympanic cavities, etc., are devoid of them. The mucus corpuscle seems to be formed by a sort of budding of the epithelial cell, part of the contents being expelled or transuded outwards, an open cell being left behind.

This mucus is found in the mouth, in the stomach and intestine, in the bile, urine, and synovia, in nasal and bronchial secretion, and in certain tumors (myxomata).

Properties.—Mucus is very variable in its characters and reactions, but always gives somewhat of a ropy consistency to the fluids containing it. Mucus is generally bright and translucent, but sometimes more or less opaque: it may be colorless, white, yellow, or greenish. The stringy character possessed by mucus depends on the presence of mucin, of which less than 1 per cent. is capable of imparting this property to the fluid in which it is present.

Although the mucus obtained from different parts varies, yet this mucin, its important constituent, is always the same.

Mucus serves to protect and cover surfaces, and in the case of buccal mucus it possibly aids the saliva in its action upon sugar; it serves also as a means for removing from the body certain organic and inorganic excrementitious materials.

Buccal mucus is a transparent, viscid, and alkaline liquid, holding epithelial cells and mucus corpuscles in suspension; *stomachal mucus* is thready, grayish, and alkaline; *intestinal mucus* is grayish, viscid, finely striated, alkaline, and rich in fatty particles and mucus corpuscles; *vesical mucus* gives a cloudy appearance to urine (Book IV., Chapter XXIV.); *vaginal mucus* is slightly viscid and always acid; that of the *neck of the uterus* is slightly viscid or gelatinous, grayish, transparent, and alkaline.

In the normal state very little mucus is formed, but in mucus catarrh it is produced in large amount. It is then clearer and more alkaline than normal, but at a later stage it becomes thicker, and in addition to abundance of epithelial cells we find mucus corpuscles in great numbers, as well as large granular exudation corpuscles, leucocytes, and fatty and proteid granulations.

There appears to be an abundant secretion of mucus during digestion.

Composition.—It generally contains mucus corpuscles similar to, if not identical with, the pale corpuscles of the blood, fine fatty granules, and sometimes crystals of cholesterin, and consists mainly of water holding in solution 4 to 5 per cent. of solids made up of mucin, traces of albuminoids, extractives, fats, and mineral salts.

Analysis of Mucus.

	Tracheal.	Nasal.	
	(Wright.)	(Berzelius.)	(Nasse.)
Water	95·6	93·37	95·56
Solids	4·4	6·63	4·44
Mucin	3·2	5·33	2·37
Extractives	0·4	1·04	0·98
Fats	—	—	0·28
Inorganic salts	0·5	0·56	0·81
Chlorides, carbonates, sulphates, and phosphates of soda and potash.			

The pyin of pus differs from the mucin of mucus in being precipitated by mercuric chloride and neutral acetate of lead, and its precipitate with acetic acid is insoluble in excess. From chondrin it is distinguished by its precipitate with alum being insoluble in excess.

Small mucus calculi are sometimes met with, consisting of mucin, fat, and phosphate and carbonate of lime and magnesia.

CHAPTER XIV.

METHODS FOR THE EXAMINATION OF SEROUS FLUIDS.

Two methods are given. By means of the first the albuminoid constituent may be readily determined, and by the second the examination

nation may be made with more completeness not only for albuminoids, but also for numerous other organic and crystalline constituents.

I. Qualitative Analysis for some of the Constituents of a Serous Liquid (*after* Hoppe Seyler).

1. Mix part of the liquid with 10 to 20 times its volume of water, add a few drops very dilute acetic acid, and then pass a continuous current of carbonic acid gas through the mixture and let it stand; if a flocculent precipitate forms, then a globulin or alkali albumen is present.

2. The above flocculent precipitate is divided into two parts. (*a*) Add to one of these a little strong sodic chloride solution; if the precipitate dissolves the liquid contains *myosin* or an analogous body. (*b*) To the rest of the precipitate add hydrochloric acid $\frac{1}{10}$ per cent.; if a solution occurs the precipitate may be *myosin*, *fibrinogen*, or *casein*.

3. Boil the liquid decanted from the precipitate obtained in 1: a coagulum indicates serum albumen.

4. Add to some of the serum a few drops of defibrinated blood (obtained by squeezing a blood clot), stir well, and lay aside in a moderately warm place for 24 hours: a coagulum indicates *fibrinogen*.

5. To a portion of the original liquid add a little pericardial serum (ox), and if a coagulum appears it is due to the presence of fibrinoplastin.

6. To a little of the liquid add acetic acid: (j) if a stringy precipitate insoluble in excess of acetic acid or sodium chloride is formed, *mucin* is present; (ij) if the precipitate formed by the first drop or two of acetic acid dissolves in the least excess, then the precipitate is probably *paralbumin*. To confirm, precipitate a little of the original liquid with three times its volume of alcohol, filter, dissolve the precipitate in water, and let the solution stand aside; if paralbumin is present the solution gradually becomes more or less viscid.

II. Examination of a Serous Liquid (*after* Gorup Besanez).

A. Boil a portion in a test tube, acetic acid having been added.

1. *A coagulum is produced.* Divide it into two portions.

(*a*) Add a few drops of hydrochloric acid; if the precipitate disappears albumen is not present, but probably *earthy phosphates*.

(*b*) If the precipitate does not disappear on the addition of the hydrochloric acid, add more of the same acid and boil, when the precipitate will gradually dissolve with the formation of a red solution—*albumen*.

(*c*) If the first coagulum obtained on boiling is reddish, then hæmatin and globulin are probably present; digest with alcohol containing sulphuric acid, and test for these bodies (see under Blood).

2. If no coagulum is produced, proceed as follows; or if this has occurred, then use the filtrate.

(*a*) Boil, and if *only a turbidity* is produced, add acetic acid: a flocculent deposit indicates *paralbumin*. Confirm by testing with potassic ferrocyanide and nitric acid.

(*b*) Test also for *metalbumin* by adding alcohol; if a precipitate is obtained soluble in a large excess of water, then this body is present, and no precipitate will be given with potassic ferrocyanide.

(*c*) If the *fluid remains perfectly clear on boiling*, then mix a portion with potassic ferrocyanide solution: *casein or globulin* is thrown down.

- (j) Boil with a solution of calcic chloride and test with rennet: a precipitate points to *casein*.
- (ij) Neutralize the solution after it has been made acid or alkaline: a precipitate points to *globulin*.

B. To some of the liquid add *acetic acid; pyin, mucin,* and *chondrin* are precipitated.

(*a*) Test the liquid with mercuric chloride: *pyin* is precipitated. Confirm with tincture of galls and neutral acetate of lead. The precipitate with acetic acid as well as with alum is insoluble in excess.

(*b*) A turbidity may be due to *chondrin*. Concentrate some of the liquid, and if chondrin is present a jelly will form on cooling. Confirm with alum and metallic salts.

(*c*) The precipitated *mucin* gives a rosy-red coloration with Millon's reagent, and a yellow coloration with nitric acid. The precipitate with acetic acid is soluble in excess.

C. Concentrate a little to a small bulk and leave it to cool: if *gelatin* is present a jelly is formed. Confirm with mercuric chloride.

D. The original liquid, from which albumen, if present, must first be separated by boiling, is evaporated at a gentle heat to one-third its volume, then boiled, and left to cool. A *precipitate* indicates *urates*. Add acetic acid and examine under the microscope, when rhombic crystals of uric acid will be seen.

Confirm by the murexid test.

If the precipitate is not altered by the acetic acid it may be due to calcic sulphate, magnesic phosphate, or to allantoin, tyrosin, calcic hippurate, or benzoic acid.

For special methods of detection see under each of these bodies in the general text.

E. The concentrated liquid gives no precipitate when cooled. Evaporate to a syrup and leave aside for several hours; if crystals form, let the liquid stand some time longer: *kreatin, kreatinin, glycocin, leucin, allantoin, taurin, sarkosin, inosit, sodic chloride, etc.*, may be present.

First determine if the crystals are organic or inorganic by heating a portion on platinum foil, noting if any charring occurs or if a fixed residue remains; then examine the crystals under the microscope. (For identifying tests consult the text.)

F. The syrupy residue, or the mother liquor from which the crystals have been separated, is next evaporated nearly to dryness, and the residue exhausted with absolute alcohol.

(*a*) Concentrate a little of the alcoholic solution, then dilute with water, and test for *bile pigment* with yellow nitric acid (p. 178).

(*b*) Treat a second portion in the same way, but apply the test for the *biliary acids* (p. 177).

(*c*) Evaporate a little to dryness, dissolve the residue in water, and test for *sugar* with Fehling's solution.

(*d*) Evaporate a considerable portion to a small bulk, add pure nitric acid to the residue when cooled, and immerse the vessel in ice-cold water: laminated crystalline precipitate indicates *urea*.

Confirm with the ordinary tests and note if any hippuric acid is present.

(*e*) To some of the concentrated alcoholic extract add a little syrupy solution of chloride of zinc: a crystalline precipitate may be due to *kreatin* or *kreatinin*.

(*f*) Heat a portion of the concentrated alcoholic extract with oxide of zinc, filter hot, and evaporate a drop of the filtrate on a glass slide; examine the deposit: if club- or tun-shaped crystals are to be seen, then *lactic acid* is present.

G. The residue insoluble in the alcohol must be extracted with water, which takes up casein, pyin, extractives, and soluble salts; then with dilute *caustic potash*, which dissolves uric acid, hypoxanthin, and guanin; and lastly with *dilute hydrochloric acid*.

The residue may contain insoluble albuminates, mucin, and probably silica.

H. Part of the original liquid is evaporated to dryness and the powdered residue exhausted with ether. The ether extract is then to be evaporated and fats looked for.

CHAPTER XV.

EPITHELIAL STRUCTURES.

I. **Epitheliums.**—These are cellular tissues that invest such free surfaces as the skin and alimentary canal, or such closed cavities as the vascular and lymphatic systems. The cells are united together by a sort of intercellular cement, which by its reducing action on salts of silver can easily be brought into view.

Except in the scales on the surface of the skin these epithelial cells are provided with nuclei as well as with a certain amount of cell contents of a protoplasmic nature, varying much, however, with the age of the cell, but generally formed of a proteid body containing granules of different kinds in its substance, such as fat, pigment, salts, etc. If glandular epithelium is also included here we find the cellular protoplasm charged in addition with the secretion and excretion elements.

Under the epithelial tissues are epidermis, epithelium, hairs, and nails, etc., and among them we may also include the crystalline lens.

Keratin.—When one of these epithelial structures, such as horn, is finely divided and digested successively with boiling water, alcohol, ether, and dilute acids, a body remains behind of more or less inconstant composition, to which the name keratin has been applied, and which accordingly cannot be regarded as a pure chemical compound.

This keratin, which seems to be the chief component of epidermic structures, is a body closely related to albumen, yielding, like it, leucin and tyrosin when decomposed with boiling dilute sulphuric acid. It also contains sulphur, as can be shown by boiling some hair or parings of nails with a little caustic potash, and then adding hydrochloric acid, when hydric sulphide will be evolved.

Keratin is found in all the tissues developed from the ectoderm or horny layer of the embryo, and is more or less characteristic of this layer, just as hæmoglobin or globulin is of the mesoderm and mucin of the entoderm.

Keratin is an albuminoid, characterized by the large amount of sulphur contained in it, which is in part loosely combined. It is related in some respects to elasticin. *Its percentage composition* is $C = 50 - 51{\cdot}6$, $H = 6{\cdot}4 - 7{\cdot}2$, $N = 16{\cdot}2 - 17{\cdot}9$, $S = 0{\cdot}7 - 5{\cdot}0$, $O = 20 - 22{\cdot}4$.

	Hairs (Laer).	Nails (Mulder).	Epidermis (Mulder).
C	50·65	51·00	50·28
H	6·36	6·94	6·76
N	17·14	17·51	17·21
O	20·85	21·75	25·01
S	5·00	2·80	0·71

Keratin is insoluble in alcohol and ether, swells up in boiling water, and is soluble in the caustic alkalies; it is not liable to decompose, and melts when heated, burning with a characteristic smell. Under pressure and at a temperature of 150° keratin dissolves partially, sulphuretted hydrogen being evolved; and the solution is precipitated by acetic acid and potassic ferrocyanide. When boiled with dilute sulphuric acid or the caustic alkalies, keratin furnishes aspartic acid and the volatile fatty acids like acetic, butyric, and propionic, as well as ammonia, leucin (10 per cent.), and tyrosin (4 per cent).

II. **Hairs** are soluble in water under a high pressure, and the solution is precipitated by chlorine, acetate of lead, tannic acid, and the mineral acids. They are soluble also in great part in the stronger acids.

Human hair contains 4 to 5 per cent. sulphur. Silica has also been found in hair to the extent of 0·11 to 0·22 per cent. A granular brown pigment is present in the medulla of most dark hairs, but it is wanting in white and even in brown hairs.

Of *inorganic constituents* the amount is variable. Nails are rich in potassic phosphate, feathers in silica, and hairs contain 0·5 to 0·7 per cent. of ash. Of *water* the hair of the head contains 13·14 per cent.; that of the beard, 12·83 per cent.; and the nails, 13·74 per cent. But in summer the proportion of water may rise to 30 per cent.

Ash of hair may be stated to consist on the average of alkaline sulphates 23 per cent., calcic sulphate 14 per cent., oxide of iron and manganese 10 per cent., and silica 40 per cent.

Ash of Human Hair—in the 100 Parts (BAUDRIMONT).

	White.	Red.	Brown.	Black.
Sodic sulphate	22·08	18·43		
Calcic phosphate	20·53	10·29	10·13	15·04
" carbonate	16·18	4·03	5·60	4·62
" sulphate	13·57			
Silicates	12·30	42·46	30·66	6·61
Oxides of iron	8·38	9·66	10·86	8·09
Magnesic carbonate . . .	5·01	6·19	4·26	2·89
Sodium chloride	trace	0·94	2·45	3·30

III. **The Horny Structures** are insoluble in water, alcohol, and ether; soluble, with the exception of nails, in acetic acid after long boiling; they swell up also and dissolve in hot sulphuric acid.

Dilute sulphuric acid acts upon these bodies as upon albumen, causing them to yield leucin, much tyrosin, ammonia, and fatty acids. A blue or violet solution is obtained by heating them with concentrated hydrochloric acid. Nitric acid dissolves them at a gentle heat, coloring them yellow, and yielding oxalic acid as a terminal product. The younger epithelial structures are readily soluble in caustic potash, but the older ones are insoluble or nearly so. Strong boiling alkaline solutions, however, decompose them, with the formation, as with albumen, of leucin, tyrosin, ammonia, hydrogen, and volatile fatty acids.

IV. **The Crystalline Lens.**—This body differs somewhat from every other tissue in the body. It consists of a parenchyma invested by an elastic capsule. The latter is quite structureless and very elastic and brittle.

The *parenchyma* presents a layer of granular and nucleated six-sided epithelial cells that lie behind the anterior layer of the capsule and connect it closely to the chief mass of the lens, which consists of flattened hexagonal bands or fibres, about $\frac{1}{5000}$ of an inch wide, which lie in layers and run from the anterior to the posterior round the margin of the lens. Each fibre, in fact, may be regarded as a greatly elongated epithelial cell (BABUCHIN), and this accounts for the close connection between the fibres and the layer of cells behind the anterior thick fold of the capsule. Every fibre, except those of the centre, is provided with an elliptical nucleus that is situated mostly towards the margin of the lens, so that the nuclei form a curved zone constituting a prolongation of a regularly arranged series of epithelial nuclei (MEYER). All these fibres are flattened in the plane of the laminæ in which they lie, and are six-sided on cross section: by some authorities they are regarded as tubes with hyaline walls and a fluid interior.

The *density* of the lens varies, increasing towards the centre, the peripheral layers being 1·076 and the central 1·194; the *index of refraction* of the central layers is also greater than that of the peripheral.

Its reaction is alkaline, and water forms two-thirds of its substance, the solids having the following composition:—

Lens of Ox (LAPTSCHINSKY).

Albumens	34·93	Fats	0·29
Lecithin	0·23	Soluble salts	0·53
Cholesterin	0·22	Insoluble salts	0·23

Dry residue of a Lens Affected with Cataract (CAHN).

Albumens	85·37	Alcoholic extract	1·45
Cholesterin	4·55	Watery "	2·76
Lecithin	0·8	Soluble salts	2·41
Fat	1·19	Insoluble salts	1·45

The salts are made up of chlorides, sulphates, and phosphates of the alkalies, with calcic phosphate in small amount.

According to CAHN only one albumen is present—a globulin substance like vitellin. The lens, however, according to LAPTSCHINSKY, contains at least two albuminous bodies, one soluble and the other with difficulty soluble in water, but readily soluble in sodic chloride solution. According to BERZELIUS, again, if the lens is rubbed up with washed sand and then digested with water, a solution is obtained containing *crystallin* or *paraglobulin*, which separates when a current of carbonic acid gas is passed through the liquid; and is also precipitated by dilute acetic acid, and when precipitated is insoluble in water containing no air dissolved in it, but if a little oxygen is passed through the water in which it is suspended an opalescent solution is formed, which gives a coagulum when heated to 93°. In addition to this paraglobulin there is present in small amount a body resembling casein, and precipitated by the addition of very dilute acetic acid to the clear filtrate from the first precipitate; and also a third albuminoid body in the filtrate that is coagulated by heat when the two preceding bodies have been removed.

The *capsule* is of an elastic nature, but it probably contains a keratin-like body.

After death and during life a coagulation of the albumens may occur, leading to opacity; an opacity may also be produced by a separation of cholesterin crystals, of earthy phosphates, or of carbonate of lime; fatty degeneration may likewise occur, and entozoa may show themselves.

Another epithelial structure, *enamel*, should be taken up here, but for convenience sake its constitution will be given under Teeth (p. 257).

CHAPTER XVI.

CONNECTIVE TISSUES.

THE term connective tissue has been variously applied, some histologists including under it only white and yellow fibrous tissue, while others regard cartilage, bone, and dentine as being of the same nature as white fibrous tissue, and accordingly group them under the same head. As the name implies they all connect or support parts; they have also more or less of a common origin, being derived from similar embryonic cells, that develop around them a matrix or intercellular substance in which the chief developmental changes subsequently occur; and they often in parts run imperceptibly one into the other in such a way as to indicate the closest relationship.

The connective tissue is very generally spread throughout the body, supporting, binding, and investing parts and organs, and also taking an important share in general nutrition, as the whole connective tissue may be regarded as constituting a continuous system of channels, passages, interstices, and reservoirs which are in direct relationship with the lymphatic system. In areolar tissue the spaces are large and freely communicate, but in membranes similar spaces exist, though they are much smaller, constituting delicate channels. Wherever, in short, the tissue is found it presents spaces or interstices that communicate freely and form a system of lymphatic spaces. And, as this tissue penetrates into all the organs and tissues, it will be seen that the arrangement results in the tissues everywhere being placed as it were in a great lymphatic sac, just as the intestines are suspended in the peritoneal cavity (RANVIER).

As its *structural elements* connective tissue presents *cells*, *fibres*, *and a cement substance* binding the fibres together.

I. **Cells.**—These are either *fixed or amœboid*. The *amœboid* are of the nature of pale corpuscles, and may either be wandering leucocytes or buds from these or from some of the fixed cells. While some are of the size of pale corpuscles, others are much larger, and are chiefly of a rounded form, although some are oval or even spindle shaped (as occasionally found in the perivascular cellular tissue).

The *fixed cells* vary in shape, but they are generally more or less flattened. They are devoid of a cell wall, although fat cells, that are derived from them, develop cell walls at the expense of the peripheral portion of the protoplasm. The greatest number of these corpuscles consists of a granular protoplasm with a granular nucleus, and are provided with branched processes; others are more or less quadrilateral' in shape, with well-marked nuclei, but devoid of processes; others again present a fusiform appearance, though many thus described are really delicate flattened bodies seen sideways or after having shrunk. WALDEYER has also described certain other cells under the heading of connective-tissue corpuscles, as, for example, the parenchymatous cells of the suprarenal capsule, and special subendothelial groups of cells met with in the testicles. Peculiar cells, called *plasma corpuscles* on account of their peculiar richness in granular protoplasm, are likewise to be seen. They are larger than the wandering cells, and are round, oval, or spindle-shaped, and are to be found especially in the perivascular tissue and in the connective tissue of glands.

In *adipose tissue*, which consists of a series of rounded or polygonal cells ($\frac{1}{300}$ to $\frac{1}{500}$ of an inch in diameter) filled with fat, the cells may be regarded as direct derivatives of the connective-tissue corpuscles, the particles of fat gradually invading the substance of the cell, swelling it up, and compressing the nucleus and the remains of the protoplasm towards the exterior, where a membranous wall has already been developed at the expense of the protoplasm.

II. **Fibres.**—These are of two kinds—the *white*, which are very fine unbranched fibres, with indistinct outlines, lying generally in wavy, tough, and flexible, glistening bundles; the *yellow*, which in mass have a faintly yellow tint, and present well-marked outlines, owing to their refracting the light strongly, also branching and anastomosing freely. The yellow are much more brittle than the white, and under manipulation they readily break, the ends curling up and showing transverse lines of fracture. The white average $\frac{1}{20000}$ to $\frac{1}{30000}$ of an inch in diameter, though they are frequently met with as fine as $\frac{1}{50000}$; and the yellow are about $\frac{1}{10000}$ to $\frac{1}{13000}$.

Acetic acid swells up the white fibres, removing all appearance of fibrillation, while it has no such action on the yellow or elastic fibres.

Both sets of fibres are generally associated together, but one or other greatly predominates, so that while in tendons and ligaments, for example, the white fibres are the chief constituent elements, in the ligamentum nuchæ and the true vocal cords the elastic fibres greatly preponderate. The white fibrils form bundles varying in thickness, and these bundles lie parallel in tendons and ligaments, and more or less parallel, with some interlacement nearly in the same plane, in fasciæ and membranes, while in areolar tissue the bundles lie loosely interlaced in different planes, and in the cutis and in mucous and serous membranes the interlacement is much closer and more complicated. The elastic fibres, and the connective-tissue corpuscles lie between and around the white bundles.

The elastic tissue may also present itself in the form of close networks and transparent homogeneous membranes. The retiform tissue may be regarded as consisting of a solid plexus of fine fibrils, upon the nodes of which little connective-tissue corpuscles are usually fixed.

III. **Cement.**—The fibres are held together in bundles by a transparent substance, which is soluble in lime or baryta water, and precipitable therefrom by acetic acid, this precipitate being *mucin*. Reference has already been made to the affinity of this cement substance for silver salts.

Classification.—Four varieties may be distinguished:—

1. *Fibrillar Connective Tissue.*—(*a*) *White fibrous*, fasciculated, as in ligaments and tendons; or membranous, as in fasciæ, aponeuroses, etc. (*b*) *Elastic*, also in fasciculated and membranous forms, as the ligamenta subflava, true vocal cords, and capsules of lens and lungs.

2. *Homogeneous Connective Tissue* occurs chiefly in the form of membranes, as the hyaloid membrane of the eye, the capsules of Graafian follicles, etc.

3. *Mucous or Jelly-like Connective Tissue* exists chiefly in the embryonic condition, and is made up of a soft, transparent fundamental substance, in which lie connective-tissue corpuscles. Examples are found in Wharton's jelly of the umbilical cord of the young embryo and the vitreous humor of the eye.

4. *Reticular or Retiform Connective Tissue* consists of a close network of fine branched fibrils, upon the nodes of which little connective-tissue corpuscles are flattened out. It used to be described as a network formed by the

branched processes of connective-tissue corpuscles. Examples are met with in the framework of lymphoid tissues and the neuroglia of the central nervous system.

Chemical Composition.—The white fibrous tissue is made up of *collagen*, a body that furnishes gluten or gelatin when boiled in water; and the elastic tissue yields *elastin*. These bodies have already been described (see pp. 124–129). In their developing fœtal condition the white fibres yield *mucin* (p. 127) instead of gelatin, in which respect they resemble the mucous and retiform tissues.

CHAPTER XVII.

CARTILAGE.

CARTILAGE consists of cells and intercellular substance, by the latter of which it is essentially characterized. The cells possess no distinctive appearance, their only specific property being the possession of rings of intercellular substance; in their early or active condition they contain glycogen, while in their inactive period particles of fat present themselves. In the adult state each cell is provided with a capsule, which is of the same nature as the matrix, but it is devoid of this covering in its young condition.

All cartilages, with the exception of the articular, are covered on their free surface by a fibrous membrane, the perichondrium, between which and the intercellular substance a very close union exists.

Classification.—In addition to fœtal cartilage there is cellular cartilage, in which little or no intercellular substance exists; hyaline cartilage, in which the intercellular matrix is more or less clear and free from fibres; and fibro-cartilages, in which the matrix is pervaded by fibres.

I. *Cellular Cartilage.*

II. *Hyaline Cartilage.* 1. *Temporary.*—The cells are small and angular, and exhibit no definite arrangement unless when the cartilage is about to undergo ossification, when they increase in size, multiply by endogenous division, and arrange themselves in rows perpendicular to the line of ossific deposit.

2. *Articular.*—Free surface devoid of perichondrium, surface cells flattened in the direction of the surface, and lenticular in shape, deep cells columnar and perpendicular to the surface, and the intermediate cells more or less rounded.

3. *Costal Type.*—Free surface covered with perichondrium; surface cells small and flattened in the direction of the periphery, and forming a thick layer; the deeper cells larger and more rounded, and the deepest cells larger still, and more or less elongated, but exhibiting only a slight tendency to be arranged with their long axes perpendicular to the surface.

(*a*) Costal cartilages.
(*b*) Ensiform cartilage.
(*c*) Cartilages of larynx, trachea, and bronchi.
Nasal cartilages.

III. *Fibro-Cartilages.* 1. *White Fibro-Cartilages.*—The matrix is composed of connective-tissue fibres. Interarticular fibro-cartilages, cartilage deepening joints (as the glenoid and cotyloid), intervertebral discs, etc.

2. *Elastic Cartilages.*—The matrix contains networks of fine elastic fibres. Ear, epiglottis, Eustachian tube, and the small cartilages of the larynx.

Chemical Characters.—When the permanent cartilages are boiled we obtain *chondrin* as the product (see p. 126), this being derived from the intercellular substance and the capsules, but not from the cells. A somewhat similar body is obtaintd by boiling the cornea. The cartilage cells themselves are not made up of ossein or chondrin, but contain a coagulable globulin albumen, which gives a purple-red color when treated with sulphuric acid and sugar, and a mahogany brown to a bluish violet with iodine (particularly the young cells). Fatty granules are often present, especially in the old cells.

The intercellular or ground substance of *hyaline cartilage* consists of *chondrogen* and yields chondrin on boiling; the matrix of the connective tissue or fibro-cartilages consists of *collagen*, and yields gelatin on boiling; while by boiling the elastic cartilages only a part of the intercellular substance is dissolved, furnishing gelatin, the rest remaining insoluble and long unaltered by caustic potash, acetic or sulphuric acid.

Composition (HOPPE SEYLER).

	Costal Cartilage.	Articular Cartilage.
Water	67·67	73·59
Organic matter	30·13	24·87
Mineral constituents	2·20	1·54

Costal Cartilage—Man, æt. 20 (FROMMHERTZ and GUGERT).

Water	62·00
Chondrin	33·26
Fat	1·33
Salts	3·40
Sodic carbonate	1·19
" sulphate	0·82
Calcic carbonate	0·62
Sodic chloride	0·28
Magnesic phosphate	0·23
Calcic "	0·14
Sodic "	0·03
Potassic sulphate	0·04
Oxide of iron	0·03

Ash of Cartilage—Variation with age (BIBRA).

In a child ½ year old	2·24	per cent.
" " 3 years "	3·00	"
" girl æt. 16 years	7·29	"
" woman æt. 25 years	3·92	"
" man " 40 "	6·10	"

Ash of Costal Cartilages (BIBRA).

	Child, æt. 3 years.	Man, æt. 22.	Man, æt. 40.
Potassic sulphate	48·68	26·66	79·03
Sodic "	10·93	44·81	1·22
" chloride	7·18	6·11	1·95
" phosphate	3·00	8·42	0·93
Calcic "	21·33	7·88	13·09
Magnesic "	8·88	4·55	3·78

Although chondrin has already been referred to, the opportunity may here be taken to compare its percentage composition with that of several allied bodies:—

	C.	N.	H.	O.	S.
Albumen . .	52·7 to 54·5	15·4 to 16·5	6·9 to 7·3	20·9 to 23·5	0·8 to 2·0
Collagen . .	50·02	18·06	6·75	24·59	0·58
Chondrin . .	50·0 .	14·4	6·6	28·4	0·6
Mucin . . .	49·5	9·6	6·7	34·2	
Elasticin . .	55·5	16·7	7·4	20·4	
Keratin . .	50 to 51·6	16·2 to 17·9	6·4 to 7·2	20 to 22·4	0·7 to 5·0

Through the action of sulphuric acid albumen, keratin, and mucin furnish leucin and tyrosin, but chondrin and elasticin only yield leucin.

CHAPTER XVIII.

BONE.

Bone is one of the indifferent or mechanical tissues of the body. It differs somewhat in appearance, as well as in chemical composition, in different parts of the body.

General Constitution of Bone considered Histologically.—Bone consists of a *series of layers called lamellæ*, which are arranged round *spaces of different kinds*. These spaces are the *Haversian canals*, the *cancelli*, and the *medullary canal*. The Haversian canals form a comparatively close network of short curved tubes throughout the substance of the compact bone, and thus establish a free communication between the exterior of the bone and the large central or medullary cavity. Towards the ends of the same bones some of the Haversian canals open up into the cancellated spaces, which may be regarded merely as dilated Haversian canals, while others form dilated loopings and curved arches beneath the articular cartilage. Contained in these canals are the blood vessels, and in the largest of the canals and in the other spaces we have in addition red and yellow marrow. The blood vessels communicate freely with those of the membrane covering the exterior of the bone, the *periosteum*, and with those of the *endosteum* in the interior of the bone.

The lamellæ form concentric layers round all these spaces, and where the latter are small and regular, as with the Haversian canals, the lamellæ are numerous, and constitute the so-called Haversian systems; but where the spaces are large and irregular, like the cancelli, there is not the same uniformity in the arrangement of the lamellæ, nor the same number of them present. In bone, after it has arrived at maturity, we have, further, concentric lamellæ more or less parallel with the periphery, lying round the exterior, and also more internally among the Haversian systems, although the latter are found at a much earlier period, having been formed under the periosteum, but in process of development coming to lie more internally among the subsequently-formed systems.

Between the lamellæ are a series of small oval spaces, the *lacunæ*, which contain the bone corpuscles, and from them radiate a set of very fine branching canals, the *canaliculi*, for the more complete irrigation of the bone tissue.

In living bone a certain amount of absorption of old bone, and a corresponding growth of new bone, is always going on, the former showing itself *in* the Haversian spaces, in which new bone is laid down in the form of concentric lamellæ.

Chemical Composition.—Although bone takes the place of temporary cartilage in the organism, it is derived from it neither chemically nor anatomically, the cartilage merely acting as a temporary substitute for it.

Bone consists of an organic substance, *ossein*, a modification of collagen, intimately combined with a mineral substance, the so-called *bone earth*, in the proportion of about thirty of the ossein to seventy of the bone earth. This bone earth is itself a mixture of several salts, the chief of which is tribasic phosphate of lime, $Ca_3 2PO_4$ [or, according to Hoppe Seyler, $3(Ca_3 2PO_4)CaCO_3$]; there is besides about 9 per cent. of calcic carbonate, 3 per cent. of calcic fluoride, and 1·7 per cent. of magnesic phosphate. Bone also contains water and fat. The general composition of normal undried bone without any separation of fat, marrow, or blood lymph, may be given as—

Water	50·00 per cent.	
Fat	15·75 "	
Ossein	11·40 "	
Bone earth	21·85 "	(Hoppe Seyler).

11 to 14 per cent. of the water is combined with the ossein, apparently after the nature of water of crystallization in crystals.

The composition is thus given by Heintz and Zalesky:—

	Heintz.	Zalesky.
Organic substances	30·47 to 31·12	34·56
Inorganic "	69·53 " 68·88	65·44
Ash in 100 parts—		
Calcium	38·59 to 38·56	40·13
Phosphoric acid	53·75 " 53·87	52·16
Carbonic "	5.44 " 5·51	7·81
Chlorine	——	0·18
Fluorine	1·75 to 1·58	0·23
Magnesium	0·48	0·29

Or the *ash* may be thus expressed:—

Tribasic phosphate of lime	83·89 to 87·7
" " " magnesia . . .	1·04 " 1·7
Carbonate of lime	8·9 " 13·03
Calcic fluoride (including chloride) . .	0·76 " 4·9

Pflüger obtained 5·84 per cent. CO_2 from bone ash by the action of phosphoric acid on the ash *in vacuo*.

Human bone.	Berzelius.	Frerichs.	
		Compact.	Spongy.
Ossein	32·17	31·5	38·2
Phosphate of lime	51·04	58·7	50·2
Fluoride of calcium	2·00		
Carbonate of lime	11·30	10·1	11·7
Soda, with sodic chloride	1·20		
Phosphate of magnesia	1·16		
Vessels	1·13		

Table Showing Influence of Age, etc. (**Bibra**).

	Child (two months).		Middle-aged man.	
	Tibia.	Ulna.	Femur.	Rib.
Phosphate of lime, with a little calcium fluoride	57·54	56·35	59·63	55·66
Carbonate of lime	6·02	6·07	7·33	6·64
Phosphate of magnesia	1·03	1·00	1·32	1·07
Soluble salts	0·73	1·65	0·69	0·62
Ossein	33·86	34·92	29·70	33·97
Fat	0·82	1·01	1·33	2·04

The different bones of the skeleton differ slightly one from the other in chemical composition; and the inorganic constituents are said to increase with age (Bibra); but the increase is only very slight (Frémy), the greater fragility being due to the increased porosity of the bone in old age. Compact bone is about 7 to 8 per cent. richer in inorganic constituents than spongy bone (Frerichs); and while the spongy bone is richer in water than the compact, the bones of thin people, as a rule, are richer in water than those of fat people.

A prolonged deprivation of earthy salts causes the earthy salts to diminish in the case of pigeons, and these salts, it appears, must be given in the form in which they exist in cereals and in bread (Edwards).

The tribasic phosphate in the food dissolves in liquids charged with carbonic acid gas, with the following decomposition: $Ca_32PO_4 + 4CO_2 + 4H_2O = CaH_42PO_4$ (acid phosphate of lime) $+ 2CaH_2(CO_3)_2$ (bicarbonate of lime). How the tribasic phosphate enters, or in what state it exists in the blood, it is difficult to say. It may be rendered soluble by the action of free carbonic acid, as we have just seen, or by the alkaline chlorides, or else by organic substances. The bone earth appears also to be subject to constant change in the living bones, a portion being redissolved in some of the alkaline salts of the blood and excreted by the intestine (Recklinghausen).

The *proportion of the organic and inorganic constituents* remains very constant, though it differs somewhat in different animals, and even in different parts of the same animal, of which examples have been given above. While the organic matter in human bones is about 34·56 per cent., in the ox it averages about 32·02 per cent.

Next to enamel, bone is the richest in inorganic salts of any tissue in the body.

The Marrow differs in different situations. In the shaft of long bones it is yellowish in color and resembles ordinary adipose tissue, the cells being supported by a sort of retiform tissue, and scattered among them a few true marrow cells may be found. In this yellow marrow there is about 96 per cent. of fat, with some cholesterin, and small quantities of hypoxanthin, albumen, and occasionally lactic acid. The framework supporting the softer structures yields mucin. In the cancellated ends of long bones, in the vertebræ, in short bones, and in the flat cranial bones, the marrow is reddish in color and contains few adipose vesicles; but true marrow cells, resembling pale corpuscles in many points, and like them possessing amœboid movement, are present in great numbers, as well as cells that are described as transition forms between the narrow cells and the colored corpuscles of the blood;

likewise large clumps of multinucleated protoplasm (*myeloplaxes of* ROBIN). The red marrow may have a mucous appearance, as in the case of the cranial bones.

In addition to a small proportion of fat, red marrow yields much albumen and salts, and an acid resembling lactic acid.

Red marrow acts probably like the splenic pulp in disintegrating colored corpuscles of blood, and it appears also to take part in the generation of new red corpuscles.

Pathology.—In *leukæmia* the red marrow becomes of a dirty grayish white, and in the yellow marrow formic and other fatty acids show themselves, as also numerous crystalline needles. In the early stages of this disease the red marrow often resembles raspberry jelly, while in the later stages it may appear as a bulky, purulent-like mass. In *typhus* numerous large, pale, red-corpuscle-holding cells are to be seen. In *variola* during the suppurative stage the myeloplaxes and pale cells may be greatly increased, while in *hæmorrhagic variola* the nucleated colored cells may be increased and the pale ones diminished. In *marasmus* following chronic diseases the embryonic blood corpuscles in the marrow are often greatly multiplied.

In most of the diseases of bone the inorganic salts undergo a quantitative and the organic constituents a qualitative alteration. The former shows itself chiefly in a diminution of the lime salts, as in rickets and osteomalacia, in this last disease lactic acid apparently taking part in the removal of the salts.

The *altered chemical composition in several diseases* is indicated in the subjoined table:—

Organic constituents.	Rickets—tibia. (LEHMANN).	Osteomalacia—vertebra. (PRÖSEL).	Caries—vertebra. (VALENTIN).	Necrosis. (BIBRA).	Arthritis—femur. (MARCHAND).	Chronic gout. (LEHMANN).	Osteosclerosis. (RAGSKY).
Phosphate of lime	32·04	13·25	33·91	72·63	43·00	35·16	61·47
Carbonate	4·01	5·95	7·60	4·03	8·24	8·41	
Phosphate of magnesia	0·98	—	0·39	1·93	1·01	1·31	
Phosphate of soda and sulphate of lime	—	0·90					
Soluble salts (chiefly sodium chloride)	0·75	—	3·27	0·61	2·00	2·93	0·26
Ossein, etc.	54·14	74·64	54·83	19·58	46·32	38·14	38·27
Fat	5·84	5·26	—	1·22	—	12·11	

Practical Exercises and Methods. 1. *To Show the Ossein.*—Digest a small bone for a day or two in dilute hydrochloric acid (10 per cent.) The earthy salts will be dissolved out, and what remains, while retaining the original form of the bone, will be soft and elastic. Wash it repeatedly in water, then in boiling alcohol and ether, and lastly, boil it for some time in fresh water, when it will be converted into *gelatin*, the network of vessels only remaining. The solution thus obtained is to be tested for gelatin (p. 125). On cooling, if the solution is not too dilute, it will set.

2. *To Show the Earthy Salts, or Bone Earth.*—Place a piece of bone in a clear fire and let it remain there until it becomes perfectly white. It will

retain its form, but it has become white and brittle. Powder a fragment and dissolve in a little hydrochloric acid; dilute the solution and add excess of ammonia; a white gelatinous precipitate of the *phosphates of lime and magnesia* occurs. Filter, and to the filtrate add oxalate of ammonia: a precipitate of *oxalate of lime* shows itself, indicating the presence of lime not present in the form of phosphate: it exists as carbonate, as can be shown by digesting some powdered uncalcined bone in dilute hydrochloric acid, when an effervescence of carbonic anhydride ensues.

3. *Preparation of Powdered Bone.*—Bones are cleaned, roughly broken into fragments, the spongy substance and the marrow, etc., carefully removed; then the fragments are enclosed in filter paper and reduced to powder in a mortar. The rough powder is suspended in a linen bag in a flask of water, and the maceration is allowed to continue several days, the water being frequently renewed. After having been dried at a temperature of 130° to 140°, the mass is finely powdered, digested with ether, and again heated to the same temperature. The powdered bone thus obtained is to be used in the subsequent analyses.

4. *To Show the Presence of a Fluoride.*—This body is frequently present. Smear a little wax over a piece of glass that has been heated; let it cool, and then draw some figures upon the wax, exposing the glass in doing so. Now place this piece of glass with the smeared surface downwards over a shallow leaden or platinum cup, into which some powdered calcined bone and equal parts of strong sulphuric acid and water have been placed; insert the cup in some boiling water, and after a little remove the piece of glass, and having scraped away the wax, note the corrosion that has occurred in the parts of the glass which were uncovered by the wax.

5. *To Show and Determine the Fat*, extract some of the dried bone with ether, evaporate the ethereal extract to dryness, and weigh the residue.

6. *Quantitative Analysis.* (*a*) *The Water.*—Weigh out five to ten grams of the powdered bone, dry at 100°, and then at 120°, until it ceases to lose weight. The loss gives the water.

(*b*) *The Ash and Organic Matter.*—Calcine in a porcelain crucible the dried bone obtained in (*a*) at as low a temperature as possible: the loss in weight gives the organic matter, and the residue the ash. It is well, before weighing, to saturate the calcined residue with ammonic carbonate, and then to heat again to an elevated temperature.

(c) *The Earthy Phosphates, etc.*—Dissolve with the aid of a gentle heat the ash obtained in (*b*) in as little moderately dilute hydrochloric acid as possible; add ammonia in excess to the solution; a precipitate is thrown down chiefly of phosphate of lime, with a little phosphate of magnesia and calcic fluoride. (As a trace of iron is present in old bones, if this is to be estimated the ammonia precipitate is to be treated with acetic acid, and the insoluble phosphate of iron collected on a filter, washed, dried, calcined, and weighed. With the acetic acid solution we then proceed as in ij.) Filter and wash the precipitate with water containing ammonia.

(j) *The Lime Present as Carbonate.*—To the filtrate add oxalate of ammonia or potash to complete precipitation, boil, filter, dry the precipitated oxalate of lime, then ignite and weigh it, by which the oxalate will be converted into carbonate of lime.

(ij) *The Lime Present as Phosphate.*—The ammoniacal precipitate of the earthy phosphate is to be dissolved in strong acetic acid with the aid of heat (if any portion remains undissolved, collect, dry, and calcine it, and having weighed it, estimate as pyro-phosphate), and to the solution oxalate of ammonia is added; boil and lay aside for 12 to 24 hours; collect the precipitated oxalate of lime, on a filter, wash, dry, and ignite both the precipitate and the filter. As the object of this is to convert the oxalate into carbonate of lime (as in j), care must be taken not to heat too strongly; and, in addition, in case any caustic lime may have been formed, it is always advisable to moisten the precipitate with carbonate of ammonia before drying it at a moderate heat and weighing it. From the carbonate of lime thus obtained the amount of lime can easily be calculated [$CaCO_3$ (100): Ca (40) = weight of carbonate of lime obtained : x].

(iij) *The Magnesia Present as Phosphate.*—The filtrate and washings of the last are to be evaporated to a small bulk, mixed with excess of ammonia, well stirred, boiled, and laid aside for 12 hours; it is then to be collected on a filter, washed with water containing ammonia, dried, ignited to redness, and weighed. The ammoniaco-magnesian phosphate is thus converted into pyrophosphate ($Mg_2P_2O_7$), from the weight of which the magnesia is readily obtained. [$Mg_2P_2O_7$(174) : 2MgO (80) = weight of pyrophosphate obtained : x.]

(iv) *Phosphoric Acid that was Combined with Lime.*—The washings and the filtrate still contain the phosphoric acid primarily combined with the lime. This is precipitated by adding a mixture of sulphate of magnesia, ammonium chloride, and ammonia, laying aside for 24 hours, then filtering and proceeding exactly as above. (1 : 0·216 = weight of pyrophosphate : x.)

(*d*) *The Total Phosphoric Acid Present.*—This may be estimated directly (CHANCEL). Dissolve 1 gram of the ash in a little nitric acid, warming gently; dilute with water, and add some baric nitrate and then some nitrate of silver; shake well and filter. Pass a current of sulphuretted hydrogen through the filtrate, filter, and boil the filtrate for some time, until the hydric sulphide has been expelled. By this means any sulphuric acid and chlorine that may have been present are removed. Now add to the clear filtrate a solution of bismuthic nitrate, filter, and wash the precipitated bismuthic phosphate with boiling water; dry it, and having detached it from the filter, ignite both separately; then weigh. [$BiPO_4$ (305) : H_3PO_4 (98) = weight of precipitate : x.]

(*e*) *The Carbonic Acid.*—Place 5 grams finely powdered and dried bone into a flask fitted with a desiccating tube filled with calcium chloride; now suspend in the flask a small test tube containing hydrochloric acid, and weigh the whole apparatus. (Or the acid may be placed in a stoppered burette fixed in the cork of the flask, and the drying of the gas effected by allowing it to escape through a U tube containing strong sulphuric acid.) The acid is allowed to flow slowly over the powdered bone, and the evolution of gas permitted to continue until it is completed. When this is the case, by means of the tube *d*, which has been stopped hitherto, force air through the apparatus, then weigh : the loss in weight = CO_2 (1 part CO_2 = 2·272 $CaCO_3$).

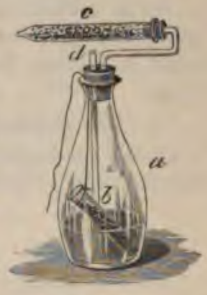


FIG. 23.—CARBONIC ACID APPARATUS.

In the flask *a* the weighed, finely-powdered bone is made into a mud with water. *b* is a small test tube containing the hydrochloric acid; *c* is a drying tube filled with fragments of chloride of calcium; *d* is a plugged tube through which air is driven when the evolution of the gas has ceased.

If greater accuracy is required, the flask is connected, as in an organic analysis, with a drying tube filled with calcium chloride, and this with a set of Liebig's bulbs containing strong caustic potash solution, to which is fixed a U tube filled with fragments of solid caustic potash. These last two pieces of apparatus are weighed before and after the experiment.

The weighed bone earth is placed in the bottom of the flask, and the hydrochloric acid is allowed to enter drop by drop from a long narrow tube fixed in the cork of the flask.

Further to avoid any error from the carbonic acid of the air, and to maintain a constant current through the apparatus, the last potash tube is in connection with a Pepy's cistern filled with water, and from which the water is allowed to escape slowly; but interposed between the two is a U tube filled with pumice stone and strong sulphuric acid, the air also before entering the flask having to pass through a similar U tube.

When all the carbonic acid gas has escaped, warm the flask for a minute or two, then disçonnect rapidly, and weigh the potash tube and bulbs.

With Geissler's apparatus also very good results are obtained.

But if the *method of titration* is adopted, then the first flask with the bone earth is connected with a second, one-quarter filled with ammonia of known strength and provided with an escape pipe filled with fragments of glass moistened with ammonia. The gas evolved by the action of the hydrochloric acid (which should here be used strong) is absorbed by the ammonia, and by heating the first flask and washing down the exit tube all the acid will be found in the ammonia, which can be directly titrated with decinormal oxalic acid.

The whole of the carbonic acid is assumed to be derived from calcium carbonate, so that the latter can easily be calculated; the whole of the magnesia estimated as magnesic phosphate ($Mg_2 2PO_4$); the amount of phosphoric acid of this being deducted from the total phosphoric acid, the difference is calculated as calcic phosphate.

CHAPTER XIX.

TEETH.

The teeth are in great part epidermic structures. A tooth consists of three distinct tissues—*dentine*, forming its chief mass, in its interior being the pulp cavity; *enamel*, investing the crown and extending some way down the neck; and *cement* or *crusta petrosa* covering the fangs.

I. The **Cement** has the structure of bone, and in its composition it is almost analogous thereto, its organic and inorganic constituents having the relative proportions of 30 : 70.

Cement of Tooth.

	Of ox (Frémy).	Of man (Bibra).
Ash (containing an average of)	67·1 per cent.	70·58 per cent.
Calcic phosphate		60·7 "
Magnesic "		1·2 "
Carbonate of lime		2·9 "

II. **Dentine.**—This body, like bone, contains an animal matrix impregnated with earthy salts.

The animal matrix is of the nature of ossein, but the walls of the canaliculi appear to have special investments of a body resembling keratin or elasticin (Hoppe Seyler). Dentine is 4 per cent. poorer in water than bone, and contains 26 to 28 per cent. organic substances.

Reckoning the carbonate and phosphate of lime together, HOPPE SEYLER gives the composition as—

$Ca_{10}CO_36(PO_4)$	72·06
$MgHPO_4$	0·75
Organic substances	27·70

According to BIBRA, the following is the composition of the dentine of men and women respectively:—

	Adult woman.	Adult man.
Organic matter—ossein and vessels	27·61	20·42
Phosphate of lime	66·72	67·54
Carbonate "	3·36	7·97
Phosphate of magnesia	1·08	2·49
Other salts (NaCl, etc.)	0·83	1·00
Fat	0·40	0·58

III. **Enamel.**—The ash averages 95 to 97 per cent.; in the young infant it varies between 77 and 84 per cent. In the dog there appears to be no organic material at all. Its average composition may be thus stated:—

Water and organic substances	3·6
Calcic phosphate and fluoride	86·9
Magnesic phosphate	1·5
Calcic carbonate	8·0

It is thus given by HOPPE SEYLER:—

$Ca_{10}CO_36(PO_4)$	96·00
$MgHPO_4$	1·05
Organic substances	3·60

Enamel and Dentine Compared—Ox (AEBY).

	Enamel.	Dentine.
Organic substance and water	3·60	27·70
Inorganic "	96·40	72·30
In 100 parts ash—		
Calcic phosphate	93·35	91·32
" carbonate	4·80	1·61
" oxide	0·86	5·27
Magnesic carbonate	0·78	0·75
Calcic sulphate	0·12	0·09
Oxide of iron	0·09	0·10

CHAPTER XX.

MUSCLE.

WE meet with two well-marked forms of this tissue in the body—*striated*, such as constitutes the voluntary muscles of the limbs, and of which a special modification forms the contractile substance of the heart; and *non-striated*, such as is met with in the uterus and in the muscular coats of the intestine.

Without going into detail with regard to the complicated structure of striated muscle, it may be briefly stated that it is made up of fibres that appear to consist of a conjoined series of short tubes formed by the sarcolemma, and that these, according to some authorities, are further divided (KRAUSE, etc.) into an immense number of little superimposed compartments, in which are contained minute bodies named sarcous rods, of whose exact chemical nature we are ignorant, the rest of the compartment being filled up with a fluid plasma, that lies not only among the rods, but is also accumulated at their ends. The rods in each compartment are arranged on the same level, so as to form a stripe that is doubly refracting, while the contractile plasma is singly refracting.

The narrow muscular fibres of the heart are made up of transversely striated, oblong, nucleated cells, which are fused together end to end; while the unstriped muscle is composed of elongated fusiform cells with oval or strap-shaped nuclei which are united together in bundles.

Properties.—In a state of rest the *reaction* of muscle is alkaline; but in coagulated muscle the reaction is acid, the acid also increasing during contraction. The acid is paralactic, but possibly also acid potassic phosphate and carbonic acid may contribute to the acidity. This increase in the acidity, as well as the accumulation of the waste products, may be the cause of the muscular fatigue experienced after continued excessive exertion. But ASTACHEWSKI has only been able to find lactic acid in muscle at rest, the acidity of the watery extract of the muscles after treatment with alcohol, in the case of paralyzed and resting muscle, having been found higher by him than that of tetanized muscle. WARREN finds that if the acidity of an untetanized limb be taken as 1, that of the tetanized limb will average 0·52. PFLÜGER explains this apparent paradox by supposing that two molecules of lactic acid condense into one with elimination of water, the acidity as measured by the power of saturating alkali being at the same time reduced to one-half.

The *density* of muscle is about 1055 in mammals—that is, the mean density of the blood.

The *color* of muscle is apparently due to the hæmoglobin contained in it independent of the blood; but in addition there has been described a yellow coloring matter soluble in ether, and presenting two absorption bands coinciding with those of oxyhæmoglobin, but not due to this body, as they are not alterable by the action of acids or of sulphuretted hydrogen (STRUVE). The name *salmonic acid* has been given to the red oily coloring principle of the muscle of the salmon, etc. (FRÉMY); its existence, however, is doubtful.

The *sarcolemma* is with difficulty soluble in acids and alkalies, and seems to be identical in some respects with keratin or elastin, but it is probably more correctly to be regarded as allied to collagen in its nature (CHITTENDEN, etc.) Under the action of dilute hydrochloric acid the muscle fibre is split into transverse discs, while that of alcohol causes it to break up into fibrils.

Changes occurring in Muscle.—Even in a *state of rest* certain chemical changes are taking place in muscle, differing only in degree from those occurring in a state of activity. The muscles also have the power of storing up oxygen while in a state of rest, particularly during sleep.

During contraction the muscle (1) becomes acid, carbonic acid being set free, and possibly also sarcolactic acid, no *immediate* increase, however, in the consumption of oxygen occurring, indicating the *independence of muscular contraction and immediate oxidation.* This is owing to the oxygen stored away by the resting muscle. As Pflüger states, the oxygen helps to wind up the vital clock. But the blood flowing away from an active muscle is poorer in oxygen and richer in carbonic anhydride than the same blood coming from a muscle at rest. In a given time, indeed, muscle work increases the absorption of oxygen and excretion of carbonic acid gas at the lungs.

2. *Heat* also is produced in muscular contraction, but this elevation of temperature really precedes the act of contraction and is not caused by it, for if work is effected by the contraction part of the heat disappears. The heat is the result of certain chemical changes occurring in the muscle.

3. Decompositions of different kinds also occur in the process of contraction, some body or bodies soluble in water being converted into others insoluble in water but soluble in alcohol; that is, *the watery extractives are diminished and the alcoholic extracts increased* (Helmholtz), showing an augmentation in the kreatin, kreatinin, and xanthin, etc.

4. Some affirm that the proteids are slightly diminished and the sugars and fats increased (Ranke). This observation, however, has not yet been fully confirmed; but it seems to be established that the glycogen of muscle is diminished by the act of contraction (Brücke and Weiss), such a decomposition as the following, in which much energy is liberated, being probable: $C_6H_{10}O_5 + H_2O = C_6H_{12}O_6$, and $C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O$. It is probable also that a *slight* increase occurs in the elimination of urea, but not an increase in any way proportional to the work done; likewise an increased elimination of sulphuric and phosphoric acids in the urine, the acidity of that fluid also being said to be raised. But it must be confessed that of the exact nature of the changes little really is known. Hermann is of opinion that an analogy exists between ordinary muscular contraction and rigor mortis, and that in both cases a complex body, which he calls *inogen*, is split up into carbonic and lactic acids and a nitrogenous residue of the nature of myosin; in the living body the myosin thus formed is redissolved as rapidly as it is generated, being reconverted, in combination with other bodies present, into the inogen, such a conversion of course not being possible in rigor mortis.

In *rigor mortis* the muscle becomes more or less opaque, loses its elasticity, is firmer to the touch, and all normal muscle currents have disappeared; its reaction also is decidedly acid, although it is frequently amphicroitic, sarcolactic and inosic acids being present, and an excess of carbonic acid being set free at the same time. A relationship appears to exist between the intensity of the rigor mortis and the amount of these acids formed. Some suppose, therefore, that these bodies result from the splitting up of a complex compound previously present. Rigor mortis, then, is characterized by the coagulation of the muscle plasma of the living muscle and by the appearance of sarcolactic acid.

Chemical Composition.

Analyses of Muscle (Bibra, Schlossberger, etc.)

Components in the 100 parts.	Pectoralis major.		Mean of human muscle.	Mean of muscle of mammal.	Muscle of birds.	Muscle of fish.	Muscle of frog.
	Man, æt. 59.	Woman, æt. 36.					
Water	72·56	74·45	73·50	72·87	73·00	74·08	80·43
Solids	27·44	25·55	26·50	27·13	27·00	25·92	19·57
Coagulated albumens (myosin, etc.) and their derivatives; sarcolemma, vessels, nerves, etc., insoluble in water . .	16·83	15·54	16·18	15·25	17·13	10·13	
Soluble albumens and albuminates; hæmoglobin .	1·75	1·93	1·84	2·17	3·13	3·61	1·86
Fat	4·24	2·30	3·27	3·71	1·94	4·59	0·10
Gelatin . . .	1·92	2·07	1·99	3·16	1·40	4·34	2·48
Kreatin . . .	—	—	0·22	0·18	0·33	—	0·28
Ash	2·68	3·57	3·12	1·14	1·30	1·49	

Non-striated muscle appears to have nearly always an alkaline reaction, and its ashes are richer in salts of soda than in those of potash. The *analysis of non-striated muscle* is thus given by Chittenden:—

Water	79·60	to	80·25
Solids	20·40	"	19·75
Ash	1·26	"	1·22
Albuminous bodies	15·68	"	15·04
Ethereal extractives	0·33	"	0·24
Non-nitrogenous bodies	3·25	"	3·12
Glycogen	2·43	"	1·98
Glycocin	0·71	"	0·39

The Gases of Muscle.—These are in part dissolved in the muscle plasma, and in part combined with its salts.

CO_2	14·4 per cent.	
N	4·9 "	
O	0·09 "	(Szumowski).

By bringing living muscle into boiling water, and then passing it through air, and treating it with phosphoric acid, a mean of 7·2 per cent. CO_2 was obtained by Stirizing, of which one part was combined. But the amount of CO_2 appears to vary according to the mode of preparation of the muscle, as when tetanized and quickly cooled it yields 6·6 per cent., but 13·5 per cent. when tetanized and cooled slowly; only 2·7 per cent. when washed, 2 per cent. when warmed for some time, and 15·4 per cent. when neither warmed nor washed.

The *solids* of muscle vary on an average from 21 to 26 per cent. in mammals, and 22 to 28 per cent. in birds, and about 20 per cent. in cold-blooded animals. In mammals the solids, in addition to those tabulated above, may be thus stated:—

	Per cent.		Per cent.
Glycogen	0·4 to 0·5	Potash	0·3 to 0·4
Kreatin	0·2	Soda	0·04
Sarkin	0·02	Lime	0·01
Xanthin and hypoxanthin	0·02	Magnesia	0·04
Taurin (horse)	0·07	Sodic chloride	0·01 to 0·004
Lactic acid	0·05	Oxide of iron	0·01 " 0·003
Phosphoric acid	0·3 to 0·5		

The different muscle constituents may be arranged in three groups:—

I. *Nitrogenous bodies*—myosin, and two or more other proteids; extractives such as kreatin, sarkosin, sarkin, xanthin, and carnin.

II. *Non-nitrogenous bodies*—inosit, fat, glycogen, etc.

III. *Inorganic bodies*—phosphoric acid, potash, soda, magnesia, lime, etc.

I. Nitrogenous Bodies.

The living muscle contains a liquid, coagulable plasma which can be removed, and this on coagulating at ordinary temperatures separates into clot and serum, this clot (*myosin*) being the same body as is obtained from dead muscle by dilute sodic chloride solution; myosin is not therefore present in the living muscle, only its factors, so to speak.

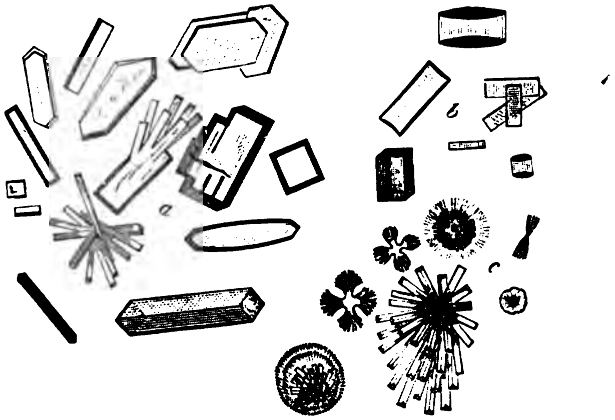


FIG. 24.—CRYSTALS OF KREATIN AND KREATININ.
a, crystals of kreatin; *b*, crystals of kreatinin; *c*, crystals of chloride of zinc and kreatinin.

By the action of acids this body is further transformed into *syntonin*. The muscle contains, in considerable amount, a body analogous to serum albumen, and coagulating at 75°; in very small proportion a soluble proteid coagulating at 45°; and a third proteid, a sort of alkali albumen, which varies in its point of coagulation (20° to 30°) according to the acidity of the serum. But it is possible that some of these may be derived from the lymph in the muscle.

The gelatin of muscle comes from the connective-tissue elements present, such as the perimysium, sheaths of nerves, blood vessels, etc., although the muscle plasma may contain collagen (HOPPE SEYLER).

A myosin ferment identical with the fibrin ferment of blood has been separated from frog's muscle (MICHELSOHN).

The muscle plasma, myosin, and muscle serum have already been described (p. 110).

The Extractives.

While these form 2 to 4 per cent., at least two-thirds of them are yet unknown. Among the nitrogenous extractives are found kreatin, sarkosin, hypoxanthin, xanthin, carnin, inosic acid, etc.

I. KREATIN, $C_4H_9N_3O_2 + H_2O$, *or* $N_2\left\{\begin{array}{l} CN \\ CH_3 \\ H_3 \\ C_2H_2O.OH \end{array}\right.$, *or* ($NH.NH_2CN.CH_3.CH_2COOH$).—It is a very weak base, but it forms crystalline compounds with several of the mineral acids; it also combines with mercuric chloride and nitrate; its crystals appear as colorless, transparent, rhombic prisms, but in the anhydrous condition it is white and opaque. Fresh muscle contains a mean of 0·2 per cent., or the solids of muscle a little more than 1 per cent. It is increased by muscular activity. Kreatin is sparingly soluble in cold water, moderately soluble in hot water, less soluble in alcohol, and insoluble in ether.

Preparation.—1. Rub up pieces of muscle with fragments of glass, and digest the mass with twice its volume of alcohol in a water bath; express the extract through linen, evaporate off the alcohol, and precipitate the watery extract with basic lead acetate; through the filtrate from this last sulphuretted hydrogen is passed to separate excess of lead, and when the latter has been removed evaporate to a syrup, from which on cooling kreatin will crystallize out.

To free it from the kreatinin that is generally combined with it, treat with chloride of zinc.

2. Rub up some Liebig's extract of meat with water and then with baryta water, filter, and remove excess of baryta from the filtrate by a current of carbonic acid gas; after filtration evaporate to one-twentieth its volume, and leave the syrup aside for several days to crystallize.

The same process may be adopted with a watery extract of fresh meat when it has first been freed from albumen by boiling.

Derivatives.—1. Boil kreatin several days with water, or for half an hour or so with a concentrated acid, and kreatinin is obtained: $C_4H_9N_3O_2 = C_4H_7N_3O + H_2O$.

2. By long-continued boiling with baryta water kreatin is decomposed into sarkasin and urea: $C_4H_9N_3O_2 + H_2O = C_3H_7NO_2$ (sarkosin) + CON_2H_4. The urea decomposes in part still further into carbonic anhydride and ammonia.

On the other hand, by boiling for several hours two parts of sarkosin with one part freshly prepared cyanamid, kreatin will crystallize out on cooling: kreatin may accordingly be regarded as methyl glycocyamine.

To determine its presence, convert it into kreatinin by boiling it for half an hour or so with sulphuric acid, then neutralize, and precipitate with chloride of zinc.

II. SARKOSIN ($C_3H_7NO_2$) may be regarded as glycocin in which hydrogen is replaced by methyl: glycocin $= \left.\begin{array}{l} C_2H_3O \\ NH_2 \end{array}\right\} O$; sarkosin $= \left.\begin{array}{r} C_2H_2(CH_3)O \\ NH_2 \end{array}\right\} O$. Sarkosin is produced by the decomposition of kreatin, this body splitting into sarkosin and urea when boiled with baryta water.

Preparation.—A hot saturated solution of kreatin is boiled with ten times its volume of baryta water so long as any ammonia is evolved, fresh baryta water being added from time to time. Then filter and precipitate the excess of baryta with carbonic acid. From the evaporated syrupy filtrate sarkosin will separate in a few days. The crystals are purified by dissolving them in excess of dilute sulphuric acid, and the solution evaporated to a syrup and well shaken with alcohol. Sarkosin sulphate separates as a fine powder, which is to be washed in cold alcohol dissolved in water, boiled with baric carbonate till carbonic acid gas ceases to be evolved, filtered from the baric sulphate, and the filtrate evaporated to a syrup. Sarkosin crystals will separate inside 24 hours.

Caffein, when similarly treated, also yields sarkosin.

Properties.—It crystallizes in colorless rhombic prisms that are soluble in water, slightly soluble in alcohol, and insoluble in ether. It combines with acids, forming soluble salts; its double salt with platinic chloride crystallizes in large yellow octohedra ($C_3H_7NO_2.HCl + PtCl_4 + H_2O$), and that with chloride of gold in rhombic tables ($C_3H_7NO_2.HCl + AuCl_3$). With acetate of copper it gives a marked blue color, forming a crystalline compound with this salt; it combines also with chloride of zinc and mercuric chloride.

III. SARKIN, or HYPOXANTHIN ($C_5H_4N_4O$), is found in muscle, generally in the proportion of about 0·02 per cent.; it is also present in the spleen, liver, thymus, and in the blood and urine of leukæmia, generally accompanying xanthin.

Preparation.—It is prepared from the mother liquor of the kreatin, which is diluted with water and then boiled with two-thirds its volume of a solution of cupric acetate. The sarkin cupric oxide is washed in cold water, suspended in hot water, decomposed with a stream of hydric sulphide, and filtered hot. The sarkin separates on cooling.

It can also be well prepared by adding gradually to a boiling saturated solution of kreatin ten times its weight of hydrate of baryta; the mixture is boiled so long as any ammonia is evolved; filter, pass a current of carbonic acid gas through the filtrate, and filter again; lay the last filtrate aside to crystallize. To purify it dissolve up the deposit in dilute sulphuric acid, evaporate to a syrup, and add alcohol. The crystalline powder is then dissolved in water, warmed with carbonate of baryta as before, filtered, and the filtrate evaporated to a syrup and then laid aside.

Properties.—Sarkin crystallizes in fine needles and is slightly soluble in hot water, but readily soluble in the alkalies and in dilute hydrochloric acid. It combines with acids, bases, and salts; with silver nitrate it forms a crystalline compound when precipitated from its ammoniacal solution by means of this body ($C_5H_2Ag_2N_4O+H_2O$). This is a more insoluble salt than the corresponding one formed with xanthin. Its hydrochloride is also less soluble than that of xanthin. It is not precipitated by ammonio-acetate of lead.

Chemical Relations.—Sarkin is closely related to xanthin and uric acid, being formed by the reducing action of sodium amalgam upon either of these bodies:

$$\underset{\text{(uric acid.)}}{C_5H_4N_4O_3};\quad \underset{\text{(xanthin.)}}{C_5H_4N_4O_2};\quad \underset{\text{(sarkin.)}}{C_5H_4N_4O}.$$

IV. XANTHIN ($C_5H_4N_4O_2$).—Mixed with hypoxanthin it is met with in different parts of the organism, as in muscle, spleen, pancreas, and liver. Its formation seems to precede that of uric acid, from which it differs in containing an atom of oxygen less; indeed, by reducing uric acid with sodium amalgam it can be obtained, or by the oxidation of sarkin. It has been found in the urinary calculi.

Preparation.—It can be prepared from the yellow crust obtained in the treatment of the extractives by dissolving this up in dilute hydrochloric acid and slowly evaporating the solution.

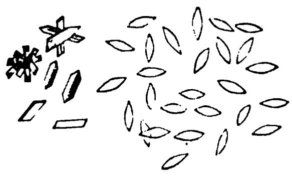


FIG. 25.—CRYSTALS OF XANTHIN. To the left are pearly rhombic tables of the sulphate.

But it is best prepared from guanin ($C_5H_5N_5O$) by dissolving this body in strong nitric acid, adding potassic nitrite in excess, and then water until a yellow precipitate is formed, which is dissolved in boiling ammonia and sulphate of iron added until a black precipitate appears. The filtrate is evaporated, and the residue, after having been washed in cold water, is dissolved in boiling ammonia, filtered, and evaporated to dryness.

Properties.—1. It is white and amorphous, forming microscopic granules very slightly soluble in boiling water, insoluble in alcohol and ether, and forming soluble combinations with bases; its solutions are precipitated by acids, with which it forms crystalline salts, and by the salts of copper, with which the precipitates are greenish.

2. Xanthin dissolves in boiling ammonia, and the solution is precipitated by chloride of zinc, cadmic chloride, and acetate of lead; silver nitrate also throws down from this ammoniacal solution the gelatinous compound $C_5H_2Ag_2N_4O_2+H_2O$.

If the xanthin is dissolved in some warm dilute nitric acid and silver nitrate added, little flocculi will separate on cooling: $C_5H_4N_4O_2+AgNO_3$.

3. Phosphomolybdic acid gives with it a voluminous yellow precipitate soluble in dilute acids.

4. When evaporated to dryness with nitric acid a yellow residue is obtained, which becomes reddish yellow on the addition of soda, changing to a violet on heating.

V. CARNIN ($C_7H_8N_4O_3+H_2O$).—American extract of meat contains about 1 per cent of this body, but it has not yet been found in fresh meat.

Carnin has a pulverulent, chalky appearance; it is insoluble in alcohol and ether, but soluble in boiling water, its solution being precipitated by subacetate, but not by the neutral acetate of lead. It combines with warm hydrochloric acid, its hydrochlorate, $C_7H_8N_4O_3.HCl$, forming brilliant needles, and combining readily with platinic chloride with the production of a double salt; with silver nitrate it also gives a white flocculent precipitate $(C_7H_8N_4O_3)_2.AgNO_3$, which is insoluble in ammonia and nitric acid.

Like sarkin, carnin is an imperfectly oxidized decomposition product. $C_7H_8N_4O_3=C_5H_4N_4O$ (sarkin) + $C_2H_4O_2$ (acetic acid). It may be converted into sarkin by the action of nitric acid or bromine.

Preparation.—It is prepared from Liebig's extract of meat by boiling this with seven times its weight of water, precipitating the solution with baryta water, carefully avoiding excess; filtering, adding subacetate of lead to the filtrate, and separating the precipitate that forms, which consists of a combination of carnin and plumbic oxide. Suspend this compound in hot water and decompose it with a current of hydric sulphide, filter, and concentrate the filtrate by evaporation. The colored deposit is to be treated with silver nitrate, and, to remove any silver chloride that may form, wash the precipitate with ammoniacal water, and then with pure water; suspend again in water and decompose with hydric sulphide, filter, and digest the filtrate with animal charcoal. From the clear filtrate, when concentrated, carnin is deposited.

VI. INOSIC ACID ($C_{10}H_{14}N_4O_{11}$) has not as yet been satisfactorily determined in human flesh, but it forms about 0·01 per cent. of the muscle of cats or rabbits.

Its alkaline salts form fine needles easily soluble in water, but insoluble in alcohol, and its solutions give amorphous precipitates with copper and silver salts.

VII. The proportion of *xanthin*, as well as of uric acid, is very small, and the same may be said for the *pepsin and ptyalin ferments* that are said to exist in muscle. *Taurin* has been found in fish and horse flesh, and *leucin* in horse flesh.

GUANIN ($C_5H_5N_5O$) was originally obtained from guano, in which it exists in the proportion of about ½ to ¾ per cent.; but it has also been found in small quantities in the liver, pancreas, and muscle. It forms a white amorphous powder, easily soluble in potash, soda, and the mineral acids, but insoluble in water, alcohol, ether, and ammonia.

It is *prepared* by boiling Peruvian guano with dilute milk of lime so long as the filtrate is colored; the residue is then extracted with a boiling solution of sodic carbonate until the sodic extract is no longer precipitated with hydrochloric acid; this extract is then treated with excess of acetic acid, and the precipitate, which consists of guanin mixed with uric acid, is digested with boiling dilute hydrochloric acid, the solution filtered, and the guanin precipitated from the filtrate with ammonia. To remove the uric acid completely, repeat the digestion in the hydrochloric acid and the precipitation with ammonia.

By the action of nitrous acid guanin is converted into xanthin, $C_5H_5N_5O + HNO_2 = C_5H_4N_4O_2 + H_2O + N_2$; and when a hydrochloric acid solution is treated with potassic chromate it is decomposed into guanidin, parabanic, oxaluric, and oxalic acids, and urea.

Urea is present in muscle only in diseased conditions, as in uræmia and cholera.

II. Non-nitrogenous Bodies.

1. *Inosit*, *or Muscle Sugar* (see page 91).

2. *Glycogen*, *etc.*—The amount of this is less in tetanized than in resting muscles, less also in the muscle of the heart; but the quantity present depends somewhat on the nature of the food, and on age, for more glycogen is proportionally present in young than in old muscle. In the fresh muscles of frogs from 0·3 to 0·5 per cent. can be extracted, and in rabbits 0·4 to 0·5 per cent.

As a diastatic ferment is also present in muscular tissue, it is probable that the fermentable sugar found in muscle after death is derived from the glycogen.

3. *Fats.*—These belong in part to the muscle substance, but also, particularly the glycerophosphoric acid and cholesterin, to the nerves present in the muscle. Volatile fatty acids can likewise be extracted. A constant constituent is *paralactic acid*, which is probably combined with some of the alkalies of the muscle.

To prepare paralactic acid from muscle, dissolve Liebig's extract of meat in four parts lukewarm water, and then with constant stirring add eight parts alcohol (90 per cent.) After standing some time decant the clear supernatant liquid; distil off the spirit, and having acidified with dilute sulphuric acid shake up with ether. Distil the ether extract, precipitate with plumbic carbonate, filter, pass sulphuretted hydrogen through the filtrate, and after having boiled neutralize with carbonate of zinc: zinc lactate is formed. Evaporate until on cooling crystals begin to separate; now treat the residue with five times its volume of alcohol (90 per cent.) After some time collect the fine crystalline precipitate on a filter, wash with alcohol, and then dry it. To separate some lactate that still remains in the alcoholic filtrate, evaporate the latter, dissolve up the residue in water, and precipitate the solution several times with alcohol. By decomposing with hydric sulphide the paralactate of zinc thus obtained, filtering, evaporating the filtrate to a syrup, and then dissolving it in pure ether, the zinc can be separated by filtration. From the last filtrate the ether is distilled off and the residue dried *in vacuo*.

III. Inorganic Constituents.

1. *Water.*—Its average is about 75 per cent., being greater in cold than in warm-blooded animals; it is also more abundant in the muscles of young beasts,

diminishing towards adult life and increasing again in old age; the muscle richest in water is the continually acting heart. A proportion also seems to be maintained between the water of the blood and that of the muscles, for with a thin blood the water of muscle is proportionally greater; and the same occurs in chronic wasting diseases. In great thirst the water of muscle is said to diminish. In females and weak males the water is more abundant. Indeed, age, sex, race, activity, and alteration of diet exercise a marked influence on the chemical composition of muscle, particularly in the amount of water.

2. *Salts.*—The ash of muscle is characterized by the preponderance of potassic salts and phosphates, these forming nearly 80 per cent., and by its poverty in soda salts and chlorine. The salts of magnesia are three times as abundant as those of lime, and alkaline sulphates are present only in small amount.

In dried flesh there is about 3·5 per cent. of ash, in fresh muscle 1·07 per cent., and in boiled flesh 1 per cent. (Liebig).

Boiling produces a great change in the salts. In the following table it will be seen how much of these salts can be thus extracted (Keller):—

	In the soup. Per cent.	Remaining in the flesh. Per cent.
Phosphoric acid	26·24	10·36
Potassium	35·42	4·78
Potassic chloride	14·81	
Earthy and iron oxides	3·15	2·54
Sulphuric acid	2·95	
	82·57	17·68

Keller therefore gives this percentage composition of the *ash of muscle*:—

Phosphoric acid	36·60	Iron and earthy oxides	5·69
Potassium	40·20	Sulphuric acid	2·95
Potassic chloride	14·81		

The phosphoric acid is combined with the potassium, and with the earthy and iron oxides in part, and the sulphuric acid is probably present in great part as potassic sulphate.

Pathology.—Muscle is liable to different degenerations, particularly fatty, during and after certain diseases and in old age. In many fevers more or less of a degeneration occurs. In fatty degeneration Liebig has found as much as 49 per cent. of fat. In chronic alcoholism the inosit is said to be increased. Urea, uric acid, and fats have also been found greatly augmented after different diseases. In cholera urea is met with in the muscles, principally those in which the most cramps have occurred, and this is possibly due to the want of a solvent medium to remove it.

Sources of Muscular Energy.—Liebig was of opinion that the proteids were the exclusive source of muscular energy, and that the urea excreted, derived from this consumption of nitrogenous material, was proportionally increased. But the experiments of most recent observers prove this theory to be incorrect (Parkes, Voit, E. Smith, Fick, etc.), and show that the oxidation of the proteid material represented by the urea excreted is much less than that required to accomplish the work done. Parkes, indeed, found no marked increase in the urea as the result of muscle work, often rather a diminution in its amount during the period of activity, but a slight subsequent increase in its elimination.

There is no doubt, however, as to the increased elimination of carbonic acid gas at the lungs produced by muscular exercise. A man, for example, at rest consumed in the twenty-four hours 708 grams oxygen, and produced 911 grams carbonic anhydride; but when doing work the numbers were 954 grams oxygen and 1,284 grams carbonic anhydride. The urea excreted in the same time in each case amounted to 37·2 grams during the day of rest, and 37 grams during the day of activity (PETTENKOFER and VOIT).

The source of the energy may therefore be looked for in the non-nitrogenous foods (chiefly the carbohydrates), the muscle only acting as an apparatus in which the potential energy of these bodies becomes kinetic. HELMHOLTZ has arrived, by calculation, at the conclusion that in the human organism one-fifth of the potential energy of the material thus consumed is converted into kinetic energy—which is about twice the amount of mechanical work that can be obtained by the instrumentality of the steam engine. (See also under Urea, Book IV., Chapter VI.)

GENERAL ANALYTICAL METHODS (*after* RUSSEL, STÄDELER, *etc.*)

A. I. **Preparation of Watery Extract.**—Kill a dog or cat by decapitation, open its abdomen rapidly, and having inserted a cannula into its aorta, wash out the vessels with sodic chloride solution (10 per cent.); then cut out the thigh muscles, and mince them up finely with the help of a sausage machine. The mass is next covered with distilled water, stirred well, and filtered after twenty minutes or so through linen, compressing to assist the filtration.

II. If the extract has been made rapidly, then test a small portion as follows, by which means three albumens at least are identified:—

1. Warm a little to 20° to 30°; it will become acid, and deposit a flocculent precipitate; but if the juice is too acid no precipitate is thus obtained.
2. Add a few drops of dilute acetic, lactic, or hydrochloric acid, and note the formation of a precipitate; separate this potassic albuminate by filtration, warm up the filtrate to 47°, and a precipitate is obtained; filter and warm the filtrate to 75°, and a second precipitate appears.
3. To a third specimen add a little sodic phosphate solution, and then the dilute acid, when it will be seen that no precipitation occurs, indicating that the albumen thrown down after acidifying as in 2 is an alkali albuminate.

III. **Separation of Soluble Albumens.**—The filtrate obtained in I. is to be slightly and gradually acidulated with dilute hydrochloric or acetic acid and boiled: any soluble albumens present are throw down. The filtrate is to be used in the subsequent experiments.

IV. **Precipitate of Phosphoric, Sulphuric, and Uric Acids, of Hypoxanthin, and of the Kreatin and Gelatin in part.**—These bodies are precipitated by the addition of *baryta water* to the filtrate of III.; filter.

(*a*) Boil the precipitate some time with a *dilute solution of caustic potash*, filter, and acidulate the filtrate with *hydrochloric acid;* if a precipitate appears remove it by the addition of a few drops of caustic potash, and then add ammonic chloride: *uric acid* is precipitated as *urate of ammonia.* Filter after some time.

(*b*) The filtrate from the baryta precipitate is evaporated over a water bath, and any scum that forms on its surface is to be removed and added to the precipitate *a*; when a syrup has been formed leave it aside under cover: little prisms of *kreatinin* will be deposited. (Sometimes little semicrystalline yellow spheres of leucin may be deposited here.) Separate the crystals and add alcohol to the mother liquor until a slight cloudiness appears, then lay aside in a dry place under cover: needles or crystalline grains, consisting of potassic or baric *inosate*, magnesic *phosphate*, or *kreatin* will form.

Dissolve the deposit in warm water and add *baric chloride*; baric *inosate* is precipitated. Filter, boil the precipitate with a little dilute sulphuric acid, filter, concentrate the filtrate, and add alcohol; *inosic* acid is deposited.

Mix the filtrate from the baric inosate with alcohol; two layers are generally formed: decant the one from the other; the lower is generally syrupy. If it presents a gelatinous or membranous precipitate, separate it by filtration, redissolve the precipitate in water, and reprecipitate with alcohol; this precipitate is generally *dextrin* or *glycogen*.

To the syrupy liquor, after the separation of the gelatinous precipitate when present, add an equal volume of ether; two layers will generally form, as before: the lower one may contain *lactates*, *volatile fatty acids*, *and inosit*, and the upper *kreatin*, *kreatinin*, and sometimes *leucin*. Decant or separate these layers by means of a suction tube. Concentrate the upper layer and leave it aside to crystallize; if little lamellæ are formed add some cold alcohol, collect on a filter, wash them there with more alcohol, and then dissolve them in some boiling alcohol; when the alcohol cools *kreatin* separates, the kreatinin remaining in solution.

The lower stratum formed by the addition of the ether is syrupy; add sulphuric acid in excess to remove the baryta, filter, and distil the filtrate: the *volatile fatty acids* pass into the distillate, while the residue contains *sarcolactic and succinic acids*, from which they can be removed by treating it with ether. Now add alcohol to the residue left by the ether until a precipitate appears; this consists generally of crystals of sulphate of potash mixed with *inosit*, if this body is originally present.

B. The extractives may also be separated as follows (STÄDELER):—

(*a*) Reduce the muscle to small fragments and digest with spirit for some time, warm, and then express; digest the residue for several hours with water at 50°; express a second time, and unite the two extracts. Next distil off the spirit, and filter from the deposited albumen. Reduce the filtrate to a small volume by evaporation, and add neutral acetate of lead to complete precipitation; filter, and add basic acetate of lead to the filtrate; lay aside for 12 hours, to allow the precipitate to settle, and filter again. To the last filtrate add excess of mercuric acetate, and after 6 hours or so collect the precipitate on a filter. Treat the filtered liquor with a current of sulphuretted hydrogen, remove the precipitated sulphide, reduce the clear filtrate to a small volume without letting it become syrupy; lastly, spread this concentrated liquor in thin layers in a series of shallow vessels, and complete the evaporation at a temperature between 40° and 50°: an abundant precipitation of *kreatin* occurs.

(*b*) The lead precipitate obtained above is to be suspended in water and decomposed with hydric sulphide; *xanthin* and *inosit* are present in the filtrate. Boil the latter with acetate of mercury, which throws down the *xanthin*: col- [illegible] precipitate, wash it, and then suspend it in water, where it is to be de- [illegible] a current of hydric sulphide; filter, and by evaporating the [illegible] *hin* will crystallize out in yellowish crusts.

(*c*) The mercuric precipitate is suspended in water and decomposed as before with sulphuretted hydrogen; the filtrate contains *xanthin* and *sarkin*. Evaporate to a small bulk and add ammonia in excess, and then silver nitrate; collect the precipitate, wash it with ammoniacal water and afterwards with distilled water, then pierce the filter and wash down the precipitate into a small flask, where it is to be boiled with sufficient nitric acid (sp. gr. 1·1) to make a complete solution. After it has stood about 6 hours filter and collect the combination of sarkin and oxide of silver that has been deposited; to the filtrate add ammonia in excess, and a yellowish flocculent precipitate is obtained of a combination of the same oxide with *xanthin*.

C. Liebig's extract of meat may be advantageously used for the preparation of most of the extractives (after BRUNTON).

1. Make a watery extract of a large spoonful or so of the extract, boil it quickly in a large flask, and filter through linen to remove the *coagulated albumen;* let the filtrate cool, and add acetate of lead solution to complete precipitation, but avoiding excess, and collect the precipitate.

A. *The lead precipitate.*—(*a*) Suspend it in water, and pass a current of sulphuretted hydrogen through the liquid; filter and concentrate the filtrate on a water bath; crystals separate out gradually. Filter after some hours, and wash the collected crystals of *uric acid* with water and then with spirit.

(*b*) The *filtrate* is to be evaporated to a small bulk, its own volume of alcohol added to it, and gently warmed if a turbidity shows itself. Lay aside for several days, and *inosit* may crystallize out; if no crystals appear add ether; if crystals are still absent evaporate nearly to dryness, and after the addition of a drop of nitric acid complete the evaporation; moisten the residue with calcic chloride solution, and on again evaporating to dryness a rosy red spot will indicate *inosit*.

B. *The Filtrate from the Lead Precipitate.*—Precipitate any lead present with sulphuretted hydrogen and filter.

(*a*) The filtrate is to be concentrated to a thin syrup, and then laid aside for several days. Crystals of *kreatin* will separate; decant the supernatant liquid, and to precipitate the rest of the kreatin add to it 2 or 3 times its volume of alcohol (88 per cent.) Collect all the crystals on a filter and wash them with spirit, then dissolve them in a little hot water, and on the solution cooling transparent oblique rhombic prisms of kreatin will be obtained.

(*b*) The alcoholic filtrate from the precipitated kreatin is to be evaporated to remove the alcohol, next diluted with water, ammonia added, and then an ammoniacal solution of silver nitrate; *sarkin or hypoxanthin* is thrown down as a flocculent precipitate, which is to be allowed to subside, and after having been washed several times by decantation with water containing ammonia it is to be collected on a porous filter and again washed; now, making a hole in the bottom of the filter, wash the precipitate into a small flask with nitric acid (sp. gr. 1·1). The flask is next to be boiled, and more nitric acid added, if necessary, to effect complete or nearly complete solution. Transfer the clear solution to a beaker, where it is to stand for several hours, when a double salt of silver and sarkin will crystallize out. Decant the supernatant liquid (*c*), and, having washed the crystals with ammonio-nitrate of silver, suspend them in water, and decompose them with a current of sulphuretted hydrogen. Filter, and evaporate the filtrate; *sarkin* crystallizes out.

(*c*) To the decanted liquid add ammonia in excess, and a double salt of xanthin and silver nitrate will fall as a flocculent precipitate; this, after having been washed by decantation, is to be suspended in boiling water and decomposed with hydric sulphide. The filtrate, when evaporated, gives a scaly film of *xanthin*.

CHAPTER XXI.

NERVE.

THERE is still much doubt and uncertainty, as well as difference of opinion, as to the true chemical constitution of nerve substance, particularly as to which are real nerve constituents and which only decomposition products or mere mixtures. With this very vexed and complicated question I shall try to deal as clearly and yet as briefly as possible.

Histologically the nervous tissues consist of nerve cells, nerve fibres, and of a supporting framework that may present itself as white fibrous tissue peripherally, or as the retiform neuroglia throughout the nerve substance.

The *nerve cells* are little masses of protoplasm, more or less irregular in outline, and provided with branching processes, each also possessing a large, well-marked nucleus and nucleolus. The protoplasm is granular around the nucleus, but striated towards the periphery. Of the processes given off all branch, with the exception of one, which is usually thicker than the rest, and said to be continuous with the nucleus, the so-called axis-cylinder process of Deiters. These nerve cells generally lie in groups, as we see in the anterior horns of the gray substance of the spinal cord, or in layers, as in the gray substance of the cerebrum.

The *nerve fibrils* (1) with which these cells are connected are generally either directly or indirectly associated together so as to form naked bundles (2), which are to be found as such in the gray matter, or invested with a medullary or myelin sheath (3), as in the white substance of the nerve centres; or covered with a fibrous sheath alone (4), as in the sympathetic nerve fibres; or provided with the double investment of medullary sheath, and outside this the fibrous or primitive sheath (5), as in the ordinary peripheral nerves of the body. A nerve, it may be said, is formed of one or more bundles of the last two kinds of nerve fibres associated together in varying proportions.

The myelin is half fluid in the living nerve; it swells up in water and is soluble in alcohol, ether, and spirits of turpentine, and consists of cholesterin, lecithin, cerebrin, albumen, and some fatty bodies. Osmic acid stains the myelin sheath black, and sulphuric acid gives it a reddish tint, while the axis cylinder reduces chloride of gold solutions, is stained red by carmin, and is dissolved by ammonia.

The term *gray substance* is applied to the periphery of the brain, the central mass of the spinal cord, and to the ganglionic masses scattered at the base of the brain, as well as elsewhere in the body. This gray substance consists essentially of the nerve cells, while the white substance, that as a rule forms the great mass of these centres, is made up of fibres.

According to MEYNERT a *vertical section of the cerebrum* presents 5 layers —(1) a *connective-tissue layer* on the surface, very thin in man and the higher animals; only very few nerve elements are present; (2) a narrow layer of *small pyramidal cells* closely arranged; (3) a broad vertically striated band, in which lie large and small pyramidal cells, giving off numerous ramified branches; (4) a layer of *granule-like corpuscles;* (5) beneath this a layer twice as broad, with *large spindle-shaped cells* scattered through it. The vessels as well as the ganglion cells are surrounded by lymph spaces (HIS), and the arteries are further provided with a lymph space between their tunica adventitia and media (VIRCHOW, ROBIN).

The foliated gray substance of the cerebellum has also (1) a layer of the nature of *connective tissue on the surface*, intermixed with some delicate nerve fibrils; beneath this a (2) *row of ganglionic flask-shaped cells of large size*, which communicate by lateral processes, and send off processes outwards and inwards, and then (3) a *thick nuclear layer or zone of small round cells* presenting a granular appearance.

The Gray and White Matter.—There is much difficulty in making a complete separation of the gray and white matter. In the case of the cerebrum the proportions of these two constituents have thus been given by DANILEWSKY: gray, 37·7 to 39 per cent.; the white, 62·3 to 61 per cent,; and the superficies of the gray as 1,588 to 1,692 cm.

Chemical Composition.—A close analogy appears to exist between the composition of an egg and of the brain substance; in both there are the same richly phosphorized compounds, albuminates, and proteids, also cholesterin, and excess of phosphates and potassic chloride.

The *chief constituents will be first summarized*, and then the more important of them considered in detail.

1. **The Water** is very variable in amount, differing indifferent parts and increasing slightly with age. In general where the phosphorized fats are most abundant the water is in smaller proportion.

Mean Percentage of Water.

	Per cent.
In the whole brain	71 to 83
" gray substance of brain	84
" cerebellum	77 " 80
" medulla oblongata	74
" spinal cord	72
" white substance of brain	69
In nerves	72

2. **Albuminates.**—Chiefly potash albuminate, also a globulin-like body corresponding to myosin, which is soluble in sodic chloride solution (10 per cent.) and precipitated by saturation with the same salt. There is in addition a proteid body, probably derived from the gray matter, which is soluble in water and coagulates at 75°.

3. **Albuminoids.**—These form 7 to 10 per cent. of the fresh tissue of the brain, and somewhat more than half the dry residue of the gray substance, but only about a quarter of the white. Among these albuminoids *nuclein* is described as present (JÄKSCH) in the proportion of 0·14 per cent. (GEOGHEGAN); but some chemists regard it as an impure albuminous substance (KINGZETT).

4. **Substances Soluble in Ether.**—In white matter these amount to 15 to 17 per cent., and in gray to 4 to 7 per cent.

Ethereal Extract (BIBRA).

Compound.	Brain.	Spinal cord.		Nerves.
		Woman, æt. 40.	Man, æt. 36.	Man, æt. 39.
Cerebrin	20 to 21	30·6	23·7	3·40
Cholesterin	30 " 33	32·8	54·2	0·88
Fats	50 " 46	37·6	22·1	94·97
Phosphorized fats . .	——	——	——	0·75

The medulla oblongata and the spinal cord yield the most ethereal extractives, the corpora striata and optic thalami the least; but the age of the nerve substance affects this considerably.

The spinal cord seems to contain less phosphorus than the cerebrum, and the gray substance of the latter more than the white.

The brain of the new-born contains much less ethereal extract than the same organ in the grown animal, but its water is more abundant; or, in other words, the embryonic brain is much richer in water and poorer in cholesterin, etc., than the developed brain. Further, we find that the lower a mammal stands in the animal scale the richer is its brain in water and the poorer in ethereal extract (chiefly cholesterin and lecithin), and accordingly the nearer does it approach to the embryonic brain, whilst the higher the animal's postion the poorer is its brain in water, and the richer in the ethereal extract. Some of the constituents removed by the ether are probably compounds chiefly derived from retrograde metamorphosis, and, as this is possibly most active in the highest brains, we can readily understand why the amount of ethereal extract increases in brains of higher development. That it is indicative of activity may also be seen from the fact that the very active medulla oblongata and the continuously active spinal cord are poorer in water and very much richer in ethereal extractives than the brain substance itself. In the case of cholesterin also it has been shown (FLINT) that the blood of the carotid artery is poorer in this body than that of the internal jugular vein.

Among these extractives, in addition to those already given in BIBRA'S tables, there are *neurin*, *lecithin*, *and protagon;* of which some, like lecithin, contain phosphorus; others, like cerebrin, are devoid of it.

5. **Watery Extractives.**—Of these there are *xanthin*, *hypoxanthin*, *kreatin*, *inosit* (ox brain), *sarcolactic and succinic acids*, and sometimes *leucin* and *uric acid* or a body resembling it. Many of these extractives, it is worth noticing, are also found in muscle, indicating a parallelism in their tissue changes; they are all products of retrograde metamorphosis, but the leucin and uric acid are said only to be present in diseased conditions. It is probable that the kreatin, inosit, xanthin, sarkin, and lactic acid are derived chiefly from the gray substance.

6. **Salts.**—Fresh brain yields an average of 0·57 per cent. of ash (GEOGHEGAN), which consists chiefly of potassic chloride and sodic phosphate with a little potassic and magnesic phosphate, sodic carbonate, and potassic sulphate. The solid residue of the gray substance contains about 0·63 per cent. more phosphoric acid than that of the white. The phosphoric acid appears to be increased by brain work, but this is doubtful, for it is possible that while the total phosphoric acid remains constant the alkaline phosphates may be increased and the earthy phosphates diminished. The urea and carbonic acid are also said to be increased by brain work or prolonged nervous excitation, the temperature also being raised (DAVY).

As *abnormal constituents* we may find urea and leucin in excess, as also excess of fats.

Ultimate Analysis.

I. *Fresh Cerebrum*—Ox (Petrowski).

	Gray matter. Per cent.		White. Per cent.
Water	81·60		68·351
Solids	18·40		31·65
Solids in the 100 parts—			
Albumen and gelatin	55·37	to	24·72
Lecithin	17·24	“	9·90
Cholesterin and fats	18·68	“	51·91
Cerebrin	0·53	“	9·54
Substances insoluble in anhydrous ether	6·71	“	3·34
Salts	1·55	“	0·57

II. *Mean Composition.*—Chief Constituents (after Moleschott).

	Brain. Per cent.	Spinal cord. Per cent.	Nerves. Per cent.
Water	81·43	68·58	57·07
Albuminous bodies	8·63	7·49	
Ethereal extract (fat, cerebrin, cholesterin, etc.)	8·07	30·62	22·11
Salts	0·70	0·36	0·85
Potassic phosphate	0·27	0·17	0·18
Sodic “	0·23	0·08	0·13
Calcic “	0·12	0·07	0·19

III. *The Ash.*—Analysis after the separation of the Lecithin, etc. (Geoghegan).

	Percentage in fresh brain.
Potassic chloride	0·277
Sodic phosphate	0·221
Potassic “	0·047
Sodic carbonate	0·044
Magnesic phosphate	0·030
Potassic sulphate	0·024
Calcic phosphate	0·003

Breed only obtained 0·027 per cent. of ash, of which potassic phosphate constituted 55·24 per cent., and sodic phosphate 22·93 per cent.

Schlossberger found 1 per cent. in the gray substance of a calf's brain and 1·16 per cent. in the gray matter of a human brain (æt. 75).

Difference between the Gray and White Substance Chemically.—Of the solids (1) the *albumens and neurokeratin* form more than half the gray substance and only about one-fourth of the white. (2) On the other hand, cholesterin and fat constitute more than half the dry mass of the white and about one-fourth of the gray; so that the chief constituents, so far as quantity is concerned, are water and albumens in the gray, and water, cholesterin, and fat in the white substance.

(3) In addition, the gray contains about twice as much lecithin as the white, but less cerebrin.

(4) The gray is richer in mineral constituents than the white. The ash of the gray substance is alkaline, and poorer in phosphates (**Schlossberger**); but, according to **Petrowsky**, the solid residue of gray substance contains 0·629 per cent. more phosphoric acid than that of the white.

(5) The gray substance is weakly acid, containing lactic acid, the acidity increasing after death; the white substance has a neutral or slightly alkaline reaction, and is not altered by the occurrence of death (GSCHEIDLEN).

I. **LECITHIN**, $C_{44}H_{90}NPO_9$, or $C_{42}H_{84}NPO_9$.—This body is present in nerve tissue, particularly the gray substance; also in yolk of egg, semen, blood corpuscles and serum, milk, and bile, etc.

Preparation.—1. Digest the *yolk of egg* with ether, and when the residue has lost its color it is treated with absolute alcohol, and the alcoholic extract filtered; the filtrate is cooled to —10°, when a solid body separates, having the composition $C_{44}H_{86}NPO_9$; while if the filtrate is evaporated *in vacuo* a body having the composition of $C_{44}H_{90}NPO_9$ is obtained. This last corresponds to the lecithin of the brain (DIAKONOW). Or, instead of cooling down the alcoholic extract, an alcoholic solution of platinic or cadmic chloride may be added, which precipitates the lecithin; the yellow precipitate obtained, after having been repeatedly dissolved in ether and reprecipitated by alcohol to purify it from fatty matters, is decomposed by passing sulphuretted hydrogen through its ethereal solution. It is then filtered and the filtrate evaporated, when chlorhydrate of lecithin remains behind. This may be again dissolved in alcohol and ether, shaken up with oxide of silver, filtered, and after the separation of the dissolved silver by hydric sulphide filtered afresh and evaporated.

2. It may also be prepared from the brain substance. Separate the membranes and vessels from fresh brain, and rub the latter into a paste in a mortar; then digest it with a large excess of alcohol, and let it stand for 3 or 4 days, rubbing it up from time to time. Filter and add to the filtrate platinic chloride and a little hydrochloric acid. Collect the yellow flocculent precipitate on a filter, dissolve it in ether, and decompose it with a current of hydric sulphide; filter again and evaporate, when a waxy mass will be obtained.

General Characters and Relations.—The lecithins play the part of fatty bodies, and are readily decomposed. For example, if an alcoholic solution of lecithin is poured into boiling baryta water, a precipitate of phospho-glycerate, oleate, palmitate, and stearate of baryta falls, while neurin is set free, $C_{44}H_{90}NPO_9 + 3H_2O = C_3H_9PO_6$ (glycero-phosphoric acid) $+ C_5H_{15}NO_5$ (neurin) $+ 2(C_{18}H_{36}O_2)$ (stearic acid). An ethereal solution is split into neurin and distearyl phosphoric acid by the action of dilute sulphuric acid.

Lecithin may therefore be regarded as a glyceride in which a phosphoric acid residue replaces the fatty acid radicle—

$$C_3H_5\begin{cases}O(C_{18}H_{35}O)\\ O(C_{18}H_{35}O)\\ O\ PO.OH\end{cases}$$
$$OC_2H_4(CH_3)_3N.OH.$$

In other words, it is a combination of distearyl, dipalmityl, or oleo-palmityl glycero-phosphoric acid, $C_3H_5\begin{cases}(C_{18}H_{35}O_2)_2\\ O\ PO\begin{cases}N(CH_3)\\ C_2H_4.OH\\ O.OH\end{cases}\end{cases}$, with neurin, this last body being a hydrate of trimethyl hydroxylene ammonium, $N\begin{cases}(CH_3)_3\\ C_2H_4.OH\\ OH\end{cases}$ (DIAKONOW).

Properties.—The lecithin of brain forms a colorless, slightly crystalline powder, often, however, presenting itself as a white, waxy, hygroscopic solid, that is easily fusible, insoluble in water, but swelling up in it like starch and forming an emulsion which gives a flocculent precipitate with sodic chloride. It is slightly soluble in cold alcohol and ether, but easily soluble in the same fluids when warm; also soluble in chloroform and benzole. Lecithin is readily decomposed, this occurring spontaneously at 70°, and even at ordinary temperatures the same occurs when it stands some time. Its alcoholic solution acidulated with hydrochloric acid gives with platinic chloride a yellowish flocculent precipitate of the double salt; and with cadmic chloride a white flocculent precipitate.

II. PROTAGON (CEREBROTE).

Preparation.—The brain is washed by injecting water through the carotid; it is then bruised and agitated with a mixture of ether and water kept at a temperature of 0°, and frequently renewed. Alcohol is then added to the extract thus obtained, and digestion is allowed to go on some time at a temperature of 45°; filter next, and cool the filtrate to 0°. Flocculi will thus be obtained, which are to be collected on a filter, washed in ether to free them from cholesterin, the mass then dried *in vacuo* and redissolved in alcohol at 45°, filtered, and reprecipitated by reducing the temperature very slowly to 0°. This treatment is repeated several times, and a fine crystalline white flocculent precipitate is obtained (LIEBREICH).

Relations.—Protagon forms the principal part of the white substance of SCHWANN; it may be regarded as a glucoside, and lecithin as one of the products of its saponification by water. It was first described by LIEBREICH, and closely resembles FRÉMY and BIBRA'S cerebric acid and GOBLEY'S cerebrin; for a long time past it has been regarded as a mixture of lecithin and cerebrin, but some recent investigations appear to point to its chemical identity (GAMGEE), although the evidence on the other side is apparently strong.

Characters.—The formulæ $C_{116}H_{241}N_4PO_{22}$ (LIEBREICH) and $C_{100}H_{308}N_5PO_{35}$ (GAMGEE, etc.) have been assigned to it.

When crystallized from warm alcohol it forms small fine needles arranged in groups. It is insoluble in water, swelling up in it, however, in the form of a gelatinous mass; it is insoluble also in cold alcohol and ether, but is soluble in warm alcohol.

III. **KEPHALINS and MYELINS, etc.**—Other phosphorized principles besides protagon and lecithin have been described by THUDICHUM, which he classifies as kephalins ($C_{42}H_{79}NPO_{13}$) and myelins ($C_{39}H_{86}NPO_8$, etc.) They are all soluble in water, kephalin being the more soluble, myelin only slightly so; while in hot alcohol myelin is readily soluble, but kephalin to a less extent. The myelins are the more stable. They all give the Pettenkofer reaction.

In addition to these, other new combinations, such as myeloidin, myelomargarin, neurolic acid, etc., have been described by KÖHLER; but further proof is required before they can be definitely accepted.

IV. **DECOMPOSITION PRODUCTS.**—Certain of the products of decomposition of lecithin and protagon are the same, and the chief of these are glycerin phosphoric acid, neurin, and fatty acids.

(*a*) **Glycerin Phosphoric Acid**—

$C_3H_9PO_6$ or $C_3H_5(OH)_2.O.PO(OH)_2$.

It has been found in the brain, medulla of nerves, in muscle, yolk of egg, and in bile and pus; probably, however, it owes its presence to the decomposition of lecithin.

It is obtained when lecithin is decomposed by boiling it with an alkaline solution, and is said to be produced synthetically by adding equivalent quantities of phosphoric anhydride (P_2O_5) or powdered metaphosphoric acid (HPO_3) to glycerin contained in a vessel surrounded by a freezing mixture. Water is afterwards added, and baric carbonate to neutralization; the baric phosphate is filtered off, the filtrate carefully neutralized with dilute sulphuric acid, and the baric sulphate removed. Finally, concentrate *in vacuo* at a low temperature.

Properties.—The free acid forms a syrupy mass that dissolves readily in water; it is dibasic, and is precipitated by salts of baryta and lead. Its combinations with baryta and lime are insoluble in absolute alcohol, but easily soluble in water, the calcium salt [$C_3H_5(OH)_2.O.PO.O_2Ca$] being more soluble in cold than in hot water; its combination with zinc closely resembles the lactate in crystalline appearance.

The phosphorus present in nerve matter is probably in the saturated oxydized form: in this condition it seems to exist not only in glycerin phosphoric acid, but also in lecithin and nuclein.

(*b*) **Neurin** (*Bilineurin*, *Cholin*), $C_5H_{15}NO_2$, possesses the characters of an alkaloid, and it generally occurs associated with lecithin. It is identical with cholin, a decomposition product of bile.

Neurin itself results from the decomposition of protagon and lecithin, and can be obtained from brain, yolk of egg, or bile.

Preparation. 1. *From Brain.*—Wash the brain with water, then break it up, exhaust it with ether, and boil the residue with baryta water to split up the lecithin. After some hours the excess of baryta is removed by sulphuric acid, the filtrate concentrated, and then digested with alcohol. The alcoholic solution is next evaporated to dryness, and the residue treated over a hot air bath with a solution of plumbic oxide to destroy the salts of ammonia. Filter, precipitate the lead with sulphuretted hydrogen, evaporate to dryness, make an alcoholic extract, and add to this platinic chloride; on evaporation a double salt of neurin and platinic chloride is obtained. This last is washed in alcohol, dissolved in water, sulphuretted hydrogen passed through the solution, the whole filtered, and the filtrate slowly evaporated. Chlorhydrate of neurin is thus obtained, from which the neurin can be separated by treating it with silver oxide.

2. *From Yolk of Egg.*—Exhaust the yolk first with ether and then with boiling alcohol; distil the mixed extracts, and boil the residue with baryta water. Precipitate excess of baryta with a current of carbonic anhydride, filter, and evaporate to dryness. Dissolve up the residue in absolute alcohol, filter, and add platinic chloride, which throws down the neurin. From the yellow crystalline precipitate the neurin is obtained as in the first method.

Properties.—Neurin is a syrupy liquid that is alkaline in reaction and soluble in water, alcohol, and ether; it forms combinations with carbonic and sulphuric acids, and double salts with the chlorides of gold and platinum. Neurin is a most unstable body, as when heated it splits into glycol and trimethylamine, $C_2H_4(OH)_2N(CH_3)_3 = C_2H_4(OH)_2$ (glycol)$+N(CH_3)_3$ (trimethylamine). Its hydrochlorate crystallizes in colorless needles or plates insoluble in ether, but soluble in alcohol, from which solution platinic chloride throws down a yellow crystalline precipitate.

(*c*) **Cerebral Fats, etc.**—These bodies appear to result from the decomposition of more complex bodies, such as lecithin and the like. They include stearin and stearic acid, palmitin and palmitic acid, and oleophosphoric acid, etc. Many of them may be regarded as products of tissue metamorphosis.

(*d*) **Cholesterin,** $C_{26}H_{44}O$.—The brain contains 1·15 to 0·7 per cent. (Flint); in the brain of a boy (æt. 15) Benecke found 2·34 per cent., and in that of a woman (æt. 19) 2·12 per cent. According to Bibra it forms about one-third of the cerebral fat, along with the fats constituting over half the total solids of the white substance, and more than one-fifth of the solids of the gray.

To extract the cholesterin from a body like the brain divide it into small fragments and digest repeatedly with ether; decant and evaporate off the ether; treat the residue with boiling alcoholic solution of caustic potash; concentrate, adding a little water from time to time, and then shake well with ether. The ethereal solution, when decanted and evaporated, deposits cholesterin; crystallize the deposit afresh from a mixture of alcohol and ether.

V. **CEREBRIN** (*Cerebric Acid, Cerebrote, Stearoconote*), $C_{17}H_{33}NO_3$ ($C_{34}H_{66}N_2O_3$, Thudichum).—This is one of the non-phosphorized nitrogenous constituents. Besides occurring largely in the brain, it is also found in the axis cylinder of nerves, in the yolk of eggs, and in pus corpuscles, etc.

Preparation.—1. Gobley prepares it from the *yolk of egg* by boiling its ethereal solution with dilute hydrochloric acid, separating the oily layer and leaving it aside. After a time flocculi are deposited, which are dissolved in boiling alcohol, and reprecipitated, on the alcohol cooling, in a crystalline condition.

2. In the case of the *brain* the nerve substance is rubbed up with baryta water so as to form a thin milky fluid, then boiled, and the resulting coagulum extracted with boiling alcohol; the alcoholic solution on cooling deposits cerebrin and cholesterin: the latter of which is removed by cold ether. The insoluble residue is purified by repeated crystallization from boiling alcohol (Müller).

3. The residue left by the alcohol in the preparation of lecithin is to be repeatedly digested with large quantities of ether until the exhaustion is complete; now extract the hot alcohol several times and filter hot: cerebrin crystallizes out on the alcohol cooling. Filter off the alcohol and wash the crystalline precipitate with ether; then boil it for an hour with baryta water. Pass a current of carbonic acid gas, filter, and wash the precipitate with water and alcohol; then digest the precipitate with hot alcohol and filter while still warm.

The crystalline deposit may be again dissolved in hot alcohol, and after being once more allowed to settle it is washed afresh with ether and then dried.

Diakonow has obtained it by the decomposition of the protagon of brain or of yolk of egg.

Properties.—Cerebrin forms a soft, light, amorphous, moderately hygroscopic powder that is insoluble in water, swelling up in it, however, like starch when boiled; insoluble also in boiling alkalies and cold alcohol and ether, but soluble in boiling alcohol, ether, acetone, and chloroform.

Cerebrin may be regarded as a nitrogenous glucoside, as it furnishes a left polarizing unfermentable sugar when boiled with acids. It combines with bases, and its solutions are neutral and not decomposed by long boiling with water, although it is completely broken up when heated with baryta water.

Composition and Formulæ.—Although the formula $C_{17}H_{33}NO_3$ has been assigned to it by Müller, it is still uncertain whether it is a chemical compound or a mixture. The formula $C_{57}H_{109}NO_{12}$ is given to it by Geoghegan, and its percentage composition has been stated as C = 66·35, N = 2·29, H = 10·96, O = 20·40. Cerebrin prepared after Müller's process yielded Parcus the formula $C_{80}H_{160}N_2O_{15}$. In the mother liquor Parcus also obtained two other bodies, *homocerebrin* ($C_{80}H_{158}N_2O_{14}$) and *encephalin* ($C_{102}H_{206}N_{14}O_{19}$). Parcus's cerebrin, however, differs considerably from the cerebrin described by Müller both in its percentage composition and in its properties. He considers that Thudichum, in some of his compounds, must have been examining impure specimens of cerebrin, which, on the other hand, Thudichum denies, at the same time questioning the general accuracy of Parcus's results. Parcus, it may be said, further concludes that nitrogen is not removed by alcohol from cerebrin, and that the cerebrins previously described consist of mixtures of cerebrin, homocerebrin, and encephalin.

VI. **NEURO-KERATIN.**—This is the same sulphur-containing body that is found in epidermic structures, such as hair and nail. The central and peripheral nervous system are developed from the same layer of the blastoderm as the epidermis, and one point in common remains between them in the fact of their both yielding keratin.

Neuro-keratin is obtained by macerating sections of nerve tissue in an artificial digestive fluid, and then extracting the residue with dilute alkali, as follows: Exhaust finely divided gray substance of ox brain with alcohol and then with ether; dry and powder the residue, which is again boiled with alcohol and afterwards with water, when it is to be digested, first with pepsin fluid, and, after having been washed in water, again digested for 24 hours with trypsin fluid containing salicylic acid, and subsequently for six hours in fresh trypsin fluid at a temperature of 40°. The residue is washed with cold water and then with hot sodic carbonate solution, and afterwards extracted with dilute caustic soda (½ per cent.) What is left behind is treated with acetic acid, alcohol, and ether in succession. A yellow powder remains.

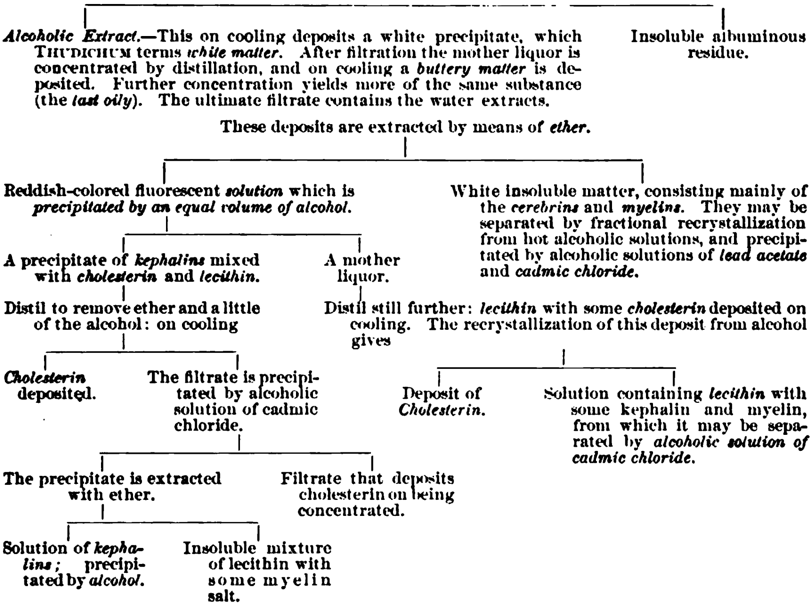
Neuro-keratin contains 2·9 per cent. sulphur and 1·6 per cent. ash; and when boiled with dilute sulphuric acid, like keratin of horn, it yields much tyrosin but less leucin. Some 15 to 20 per cent. of this body is said to be present in the brain substance.

VII. **PHRENOSIN** is a body prepared by Thudichum from the white matter that separates on cooling an alcoholic extract of the brain, by submitting it to repeated fractional crystallizations from alcohol, and precipitation of the phosphorized bodies by lead acetate and cadmium chloride. The phrenosin, together with kerasin and cerebrous acid, according to Thudichum, remain in ution and are separated by fractional crystallization from much alcohol, which, eing cooled to 28°, deposits chiefly phrenosin.

This body is white, tasteless, and odorless, and crystallizes from absolute alcohol in white rosettes. The formula $C_{41}H_{79}NO_8$ is assigned to it. By long-continued action upon it of dilute sulphuric acid at a moderately high temperature *cerebrose* ($C_6H_{12}O_6$), *sphingosin* ($C_{17}H_{35}NO_3$), a crystalline alkaloid, and *neuro-stearic acid* ($C_{18}H_{36}O_2$) are said to be formed (THUDICHUM).

The following is the method adopted by THUDICHUM *for isolating and separating the brain constituents:—*

A series of brains are freed from their membranes, rapidly washed in water, hardened in alcohol, minced and reduced to a pulp with spirit (85 per cent.), and repeatedly extracted with the same fluid, being heated for some time to 50° C.; the warm solution is filtered, and the filtrate allowed to cool. An undissolved albuminous residue remains behind.



Alcoholic Extract.—This on cooling deposits a white precipitate, which THUDICHUM terms *white matter*. After filtration the mother liquor is concentrated by distillation, and on cooling a *buttery matter* is deposited. Further concentration yields more of the same substance (the *last oily*). The ultimate filtrate contains the water extracts.

Insoluble albuminous residue.

These deposits are extracted by means of *ether*.

Reddish-colored fluorescent *solution* which is *precipitated by an equal volume of alcohol*.

White insoluble matter, consisting mainly of the *cerebrins* and *myelins*. They may be separated by fractional recrystallization from hot alcoholic solutions, and precipitated by alcoholic solutions of *lead acetate* and *cadmic chloride*.

A precipitate of *kephalins* mixed with *cholesterin* and *lecithin*.

A mother liquor.

Distil to remove ether and a little of the alcohol: on cooling

Distil still further: *lecithin* with some *cholesterin* deposited on cooling. The recrystallization of this deposit from alcohol gives

Cholesterin deposited.

The filtrate is precipitated by alcoholic solution of cadmic chloride.

Deposit of *Cholesterin*.

Solution containing *lecithin* with some kephalin and myelin, from which it may be separated by *alcoholic solution of cadmic chloride*.

The precipitate is extracted with ether.

Filtrate that deposits cholesterin on being concentrated.

Solution of *kephalins*; precipitated by *alcohol*.

Insoluble mixture of lecithin with some myelin salt.

The author has followed the above method on a small scale with very good results, though it entails the expenditure of much time and trouble.

Sonnenschein's Method for Isolating Alkaloidal Principles.—This is especially applicable to nerve substance. The reagent, which is a phospho-molybdic solution, is thus prepared: Molybdate of ammonia and sodic phosphate are dissolved together in such proportions that 30 parts of the phosphorus are present for one of molybdenum; this solution is precipitated by nitric acid, and the yellow precipitate obtained is dissolved in a strong solution of sodic carbonate. The solution is evaporated to dryness and then fused after the addition of a little nitre. When required for use it is dissolved in water, and dilute nitric acid (1 to 6) added until a golden yellow color is attained.

This reagent is added to the alkaloidal solution to complete precipitation, the precipitate filtered off and washed with acidulated water, the acid used being at first nitric and then sulphuric; afterwards it is heated with saturated baryta water, which gives a precipitate of phospho-molybdate of barium. Carbonic acid is next passed through the solution and the precipitated baryta separated by filtration, the alkaloid remaining behind in solution.

CHAPTER XXII.

THE EYE.

Retina, Aqueous and Vitreous Humor, and Cornea.

I. The *reaction* of the fresh retina is acid, but after twenty-four to forty-eight hours in the dark it is neutral.

Among the bodies that can be extracted from the retina are albumen, an albuminoid, trimethylamine, cholin, neuro-keratin, nuclein, myeloid bodies, and fats of different colors, varying between golden yellow and orange, the coloration being due to lipochrin (KÜHNE), a body allied to lutein.

CAHOURS gives the subjoined analysis of the retina:—

Water	86·52	Cholesterin	0·77
Albuminoids	6·77	Fat	0·47
Bodies resembling albuminoids	1·59	Lecithin	2·08
Alcoholic extractives	0·25	Soluble salts	0·93
Watery "	0·52	Insoluble "	0·02
		Cerebrin	traces.

The salts are chiefly phosphate, chloride, and carbonate of soda, with sulphate and chloride of potassium. The albuminoids include myosin, serum albumen, and a body resembling mucin.

The *rods and cones* contain keratin as well as an albuminous and a myeloidal body (KÜHNE). In the cones small particles of colored fat are to be seen. This colored fat is named *chromophane*, and, according to its color, is distinguished as *chlorophane*, *xanthophane*, etc., each having its own absorption spectrum. This chromophane appears to be pre-existent (KÜHNE), but whether there is only one coloring stuff present or several seems still a matter of opinion (WÄLCHI, CAPRANICA, etc.) The chromophane according to KÜHNE, is not altered by the action of alcohol, ether, benzole, chloroform, or an alcoholic solution of caustic soda. Retinæ rapidly dried *in vacuo* and rubbed up with ice-cold alcohol readily part with their chromophane; and this solution when evaporated leaves behind a reddish varnish-like residue from which water extracts a colorless crystalline substance. By making a hot alcoholic extract of a number of retinæ, filtering hot, washing with warm alcohol, and then extracting with ether, chromophane can also be obtained. The ethereal extract is next to be evaporated and the pale supernatant layer removed with a pipette from the colored residue (KÜHNE).

The retinal rods were first described by KROHN, H. MÜLLER and SCHULTZE as being red-colored in many animals. BOLL next described the retinæ of frogs and other animals that had been kept some time in the dark as presenting a purple tint, while the retinæ of animals that had been exposed to the direct sunlight were completely colorless. This red or purple tint of the living retinæ, which the exposure of light rapidly destroyed, was restored again by allowing the retinæ to rest in the dark; indeed, in the living eye this visual purple is being constantly decomposed and as constantly regenerated by the chloroidal epithelium. The red color appears to reside in the outer limbs of the rods, and to change into a yellow before disappearing. Among these red rods BOLL also described bright green rods which likewise lost their color on exposure to the light. KÜHNE'S subsequent researches establish the fact that this *visual purple*, as it has been called, is highly sensitive to light, and that images may be temporarily photographed on the retina by its means, and thus produce the accuracy of the visual impressions. Vision therefore appears to be attended with an obvious chemical attraction in the retinal rods, and it is possible that this chemical change may be propagated to the central organs; but that this change of color is not essential to correct vision appears from the absence of the visual purple from the eyes of several animals, and particularly from the most sensitive point of the human eye, the *fovea centralis*.

KÜHNE *has obtained* this vision purple by acting in the dark on the purple-colored rods with a two to three per cent. solution of the soda salt of the biliary acids, filtering, and then separating the soda salt by osmose: a myelin, purple-colored magma was thus separated, whose color is also removed by exposure to the light, first, however, becoming yellow; or, as KÜHNE expresses it, the visual purple has as its products a visual yellow and a visual white. The color is destroyed by the action of the caustic alkalies, and is taken up by alcohol, ether, chloroform, iodine, and bromine. The visual purple resists strongly the action of oxidizing and reducing agents. KÜHNE only found the visual purple in the outer part of the rods, but absent from the cones, the intensity of the coloration varying in different animals, while in some all coloration is absent. It is said to possess an absorption spectrum. Its carmine red solution in the soda salt of the biliary acids absorbs all the light rays from yellowish green to violet.

The red color presented by the retina under ophthalmic examination is due in part to this pigment, but also to the blood in the vessels.

II. In the pigmentary layer of the retina are to be met with flattened hexagonal nucleated cells filled with pigment. This fuscin pigment or melanin (1) occurs as small brownish granules that are insoluble in water, alcohol, ether, and dilute mineral acids. Its origin is supposed to be the hæmatin of the blood. It contains 0·25 per cent. of iron, and has this percentage composition:—

	(SCHERER.)	(BOROW.)
C =	58·08	54·0
H =	5·91	5·3
N =	13·76	10·1
O =	22·23	30·0
	Ash	0·6

Colored oily drops (2) are met with in the retinæ of fishes, birds, reptiles, and of some mammals. These drops are yellowish green to a ruby red color; with strong sulphuric acid the color changes to a dark violet or deep blue. The yellow and red drops contain the same pigment; and the yellow solution of the pigment in alcohol, ether, or chloroform gives two absorption bands, one at the line F and the other between F and G, somewhat resembling lutein.

Together with the vision purple there therefore appear to be three pigments in the retina.

III. (*a*) **Aqueous Humor** (LOHMEYER).—

	Per cent.
Water	98·68 to 98·64
Solids	1·32 “ 1·36
Albumen	0·12 “ 0·13
Extractives	0·42 “ 0·32
Inorganic salts	0·77 “ 0·88
Sodic chloride	0·68 “ 0·77
Potassic “	0·01 “ 0·06
“ sulphate	0·02 “ 0·01
Calcic and magnesic phosphate	0·04 “ 0·01

The aqueous humor contains serum albumen and globulin, which are present in the relative proportions of 0·06 and 0·09 per cent.

(*b*) The fluid expressed from the vitreous humor (which is itself *mucous connective tissue*) has an alkaline reaction, is coagulated by the addition of acids, alkalies, and acetate of lead, but is not coagulated by heat or by the addition of alcohol.

The vitreous humor contains only 14 per cent. solids, of which more than half are inorganic salts, together with a little mucin and traces of albumen. It has a density of 1·33.

IV. **Tears** have a simple composition (LERCH); they are clear and slightly alkaline.

	Per cent.
Water	98·0
Albumen, with traces of mucus	0·5
Sodic chloride	1·3
Other salts (as alkaline and earthy phosphates)	0·02

For the *crystalline lens* see p. 244.

V. **The Cornea** is a lamellated, white fibrous structure which is covered anteriorly by a lamellated pavement epithelium, and posteriorly by an elastic lamina. The white fibrils are extremely fine and are arranged in ribbon-like fasciculi that are closely interwoven in layers, between which are plexuses of connective-tissue corpuscles lying in a system of serous canals that form a canalicular system throughout the entire corneal substance.

The cornea, unlike ordinary connective tissue, yields chondrin, or a body analogous to it, instead of gelatin on boiling, the ground substance being chondrogen; but there is still some difference of opinion as to the actual identity of the product. A solution does not give a precipitate with acetate of lead; and the precipitate it forms of alum is not soluble in excess; neither does it furnish sugar when boiled with acids. HIS gives this analysis of the corneal substance:—

	Per cent.		Per cent.
Water	75·8	Soluble mineral salts	0·3
Chondrin	20·4	Insoluble “ “	0·1
Bodies insoluble in water	2·8		

The *protoplasm of the cells* yields myosin (KÜHNE). The cornea is minced and digested in a saturated solution of sodic chloride for 24 hours in a vessel surrounded by a mixture of ice and salt; the liquid is filtered and the myosin precipitated by the addition of excess of water. *Paraglobulin* is removed at the same time, and may be precipitated from the myosin filtrate by passing through it a current of carbonic acid gas. By macerating the cornea in water an alkali albuminate can be extracted.

CHAPTER XXIII.

THE SKIN.

THE skin consists of a superficial cellular layer, the *epidermis* (see p. 243), and of a deep thick layer, or *cutis*, which is formed of connective tissue, and, like it, yielding gelatin on boiling; it dissolves in great part in acids and alkalies, and combines with tannic acid and salts of iron and mercury.

The skin is the seat of a continuous exhalation and absorption of gaseous substances, and to these the name of *cutaneous respiration* has been given. By the perspiration the skin discharges some of the waste products of the body, eliminating vapor of water, carbonic anhydride, and a little nitrogen, and probably absorbing a little oxygen. If an animal's body, with the exception of its head, be confined in a small chamber filled with air, after some hours the air will have its carbonic anhydride slightly increased, its oxygen slightly diminished, and its nitrogen almost unaltered, the oxygen absorbed being somewhat greater than the carbonic anhydride exhaled (REGNAULT, etc.)

The *secretion work* of the skin is done by the sudoriparous and sebaceous glands; and the amount depends greatly on the state of dilatation or contraction of the blood vessels, which is under the governance of the nervous centres, their diameter being directly affected by the activity of the secretory fibres, just as is the case with the submaxillary gland.

The Sweat is the secretion of the sudoriparous glands. Normal sweat is a more or less clear and transparent fluid, having a peculiar odor and a density of 1004; possessing the character of a blood diffusate, and having dissolved in it a part of the perspiration gases, and a very small proportion of solids. The reaction is alkaline (LUCHSINGER); but as to this authorities differ, some stating it to be acid when freshly collected (probably from containing more of the fatty acids), and becoming alkaline after standing even half an hour (HOPPE SEYLER). After prolonged and especially profuse sweating, however, the reaction is neutral and finally alkaline, and at the same time the urea and mineral salts are slightly increased (FUNKE), the urea of the urine being simultaneously diminished (LEUBE).

Chemical Composition of Sweat.—The chief components are water and a very small amount of salts and of carbonic acid.

Human Sweat (after PICARD, SCHOTTIN, etc.)

	Per cent.
Water	98·88
Solids	1·12
Salts	0·57
Sodic chloride	0·22 to 0·33
Alkaline sulphates, phosphates, and lactates, and potassic chloride	0·18
Fats, fatty acids, and cholesterin	0·41
Epithelium	0·17
Urea	0·08

The mean of the solids is about 1·2 per cent. (1·8 per cent. FUNKE), ⅔ of which is organic, and about 0·33 per cent. of ash. The water varies from 97 to 99·5 per cent. While **Funke** regards the excretion of urea by the skin to be considerable, **Ranke** could not find it; **Favre**, however, estimated it at 0·04 gram in the 24 hours. **Funke** also obtained more fixed residue in the sweat of the feet than of the arms, and **Schottin** found more potassic chloride in the former than in the latter. The ammoniacal salts so often present are probably the result of decomposition of urea.

Comparing urine and sweat together, the solids in 14 litres are—

	Sweat. Grams.	Urine. Grams.
Chlorides	34·63	57·01
Sulphates	0·16	21·76
Phosphates	traces	5·38
Alkalies expressed as soda	4·18	2·49
Organic matter	22·92	139·65

Melanin is the pigment contained in the cells of the *rete mucosum*, particularly in the skin of the negro. It has already been described as existing in the pigment layer of the retina; like this body it forms fine amorphous granules that are insoluble in water, alcohol, ether, dilute alkalies, and acids, but slowly soluble in boiling concentrated mineral acids and alkalies. The name melanin, it may be said, is applied to the pigments found in the eye, skin, lymphatic glands, and lung tissue; although it is not exactly the same in all these parts, it may be uniformly regarded as a derivative of the blood pigment, with a percentage composition lying within these limits:—

C	51·7 to 58·3	Fe	0·3
H	4·0 " 5·9	O	22·0 to 35·4
N	7·1 " 13·8		

As to the *amount of water*, **Seguin** states that about 1·2 gram of fluid is given off by the skin and lungs in one minute, of which 0·7 gram comes from the skin and 0·5 gram from the lungs—that is, about 18 grains of water per minute, 11 by the skin and 7 by the lungs. In the 24 hours from 1 to 5 lbs. may be thus discharged, the average loss by the skin varying from 1 to 2 lbs. During vigorous exercise the hand and fore-arm give off, on a summer day with a temperature of 28° in the shade, about 48 grams of sweat in an hour, while with very moderate exertion in a room at 18° only about 4·3 grams in the same time. Of the large amount thus excreted by the skin the greater part passes off as insensible perspiration. In addition to exercise and temperature the quantity is affected by the dryness of the air, the amount of fluid drunk, as well as the nature and quantity of the food; but the activity of the skin depends largely on the state of the kidneys. Mental conditions also exert a considerable influence on the secretion of sweat.

The amount of carbonic anhydride is not much above 2 grams in the 24 hours, though by some authorities it is stated to vary between 4 (**Aubert**) and 10 grams (**Scharling**) in the 24 hours. It is increased by exercise and elevation of temperature. At most the carbonic anhydride thus exhaled rarely rises to the $\frac{1}{50}$ of that given off by the lungs (**Scharling**); but under ordinary circumstances it is probably much less than this, according to some observers the proportion between the carbonic acid exhaled by the skin and by the lungs not being more than 1 to 400.

Mixed with the sweat we find the **secretion of the sebaceous glands**, which varies somewhat according to the region from which it is derived.

When freshly poured out it forms an oily, half fluid mass, which on cooling appears as a white, greasy body. Under the microscope it presents fatty particles, epidermic cells, and cholesterin crystals. It consists of a casein-like albumen, olein, palmitin, soaps, cholesterin, and inorganic salts, particularly earthy phosphates, and alkaline chlorides and phosphates.

The Sebaceous Secretion.

(Pétrequin.)	
Water	10
Fatty matters (olein and stearin)	26
Soaps soluble in alcohol and water	38
Soaps soluble in water and insoluble in alcohol	14
Insoluble organic bodies	12
Lime and soda	traces

(Vogel.)	
Water	31·7
Solids	68·3
Epithelium and albumen	61·7
Fat (palmitin)	4·1
Fatty acids (butyric, valeric, caproic)	1·2
Ash	1·2

When the glands are obstructed a thick mass accumulates, consisting of altered epithelial scales, cholesterin, fatty matters, and occasionally leucin and tyrosin.

Pathology. *Skin.*—In *ichthyosis* along with keratin there is much cholesterin, a fluid and a solid fat, and hippuric acid; and silica in the ash. In *pellagra* there is also a fluid and solid fat, much cholesterin, some leucin and tyrosin, and much silica in the ash.

Sweat. The *odor* undoubtedly varies in many diseases, and sometimes characteristically so. In jaundice it may be *colored yellowish* from the presence of biliary fragments, and even stain the linen. It may have a *blue* tint from the presence of some of the indigo derivatives; hæmatin derivatives have also been observed (Robin, Foot), likewise blood in *red* sweat. *Strongly alkaline* sweat from the presence of ammoniacal salts is occasionally met with in uræmia, gout, etc.; and very acid sweat in acute rheumatism and rickets.

Urea has been found increased in the sweat in cholera and uræmia, and in the sweat of the face in scarlatinal nephritis with anuria; *sugar* in diabetes; *albumen* in acute rheumatism and forced sweating; *cystin* in cystinuria; *lactic acid* frequently in puerperal fever, and occasionally in scrofula and rickets; *uric acid* in arthritis, and *oxalate of lime* in gout.

Drugs.—Iodine and potassic iodide, tartaric, succinic, and benzoic acids may appear in the perspiration after their administration; the iodine ingested is eliminated, however, less rapidly in the sweat than in the saliva. When mercuric iodide is taken the iodine with a small portion of the mercury appears in the urine and saliva, and the mercury as perchloride in the sweat. After the use of arseniate of iron alkaline arsenites are found in the sweat, and iron in the urine. Quinine, alcohol, sulphur, and assafœtida have been recognized in the sweat after ingestion.

By covering the skin of an animal with an impermeable varnish it was stated by Röhrig that the temperature was reduced, and a peculiar pyrexia set up, owing to the retention of some of the sweat constituents, or to the consequent dilatation of the cutaneous vessels, or to some other unknown cause that may be classified as the production of abnormal tissue change. A somewhat similar pyrexia with albuminuria is said to be produced by the injection of the fresh filtered human sweat into the veins of a rabbit.

But the effects of the varnishing do not appear to be nearly so serious as Röhrig believed, for the author has repeatedly seen the experiment performed with comparatively slight results.

CHAPTER XXIV.

THE LIVER.

The liver is the largest gland in the body. Its importance is seen by the amount of blood present in it, but its close connection with the intestine is indicated by its small supply of arterial blood in proportion to the large amount of venous blood containing the absorbed products of intestinal digestion which passes through it.

In addition to the important changes it produces on the blood and its corpuscles (possibly being a generator of new blood), the liver is also the seat of the formation of bile and glycogen; it is further probable that it is one of the great centres of urea formation, although Hoppe Seyler, it should be said, has not been able to find any, or at most mere traces of urea in the liver of a recently killed dog; and he also failed to find leucin and tyrosin.

Chemical Composition.—The fresh hepatic substance is alkaline, but soon after death it becomes acid, owing probably to the development of lactic acid; it contains 60 to 70 per cent. of water, and 40 to 30 per cent. of solids, consisting, besides certain insoluble tissues, of albumens (of which three are described), fat, and salts of the volatile fatty acids, also of nuclein (in the liver cells), sarkin, xanthin, hypoxanthin, and uric acid; but urea, uric acid, and leucin, are possibly only pathological constituents. There are, in addition, traces of salts of manganese, copper, and lead. A saccharine and a butyric acid ferment are likewise met with (Pribram).

The relative proportions of the constituents vary somewhat with age:—

	Liver of a child (14 days old).	Liver of an old woman.
Water	74·14	80·63
Organic bodies	24·78	18·65
Inorganic contituents	1·07	0·71

The constituents of a human liver are thus given by Bibra:—

Water	76·17	Gelatin	3·37
Insoluble tissues	9·44	Extractives	6·07
Albumen	2·40	Fats	2·50

Of inorganic constituents Oidtmann found 1·10 per cent.

The Ash in 100 *Parts.*

Potash	25·17	Phosphoric acid	43·37
Soda	14·47	Sulphuric "	0·91
Lime	3·02	Silicic "	0·27
Magnesia	0·19	Chlorine	2·5
Oxide of iron	2·75	Lead and copper	traces

The proportion of *fat* depends more or less on the food, as its proportion is increased with a diet rich in fat. In the normal condition the fat present seems to be proportional to the fat in the rest of the organism.

The quantity of *glycogen* is very variable, depending greatly on the character of the food; normally it averages 1·5 to 2·5 per cent. In dogs fed exclusively on meat the liver may contain about 7 per cent., with a purely vegetable diet as much as 17·2 per cent., and with a mixed diet about 14·5 per cent., the glycogen disappearing when the animal is starved. According to **Seegen** and **Kratschmer** the sugar in the liver increases after death to an extent not be accounted for by the transformation of glycogen present. In the case of a young fox they found in the liver two minutes after death glycogen 0·7 per cent. and sugar 0·79 per cent.; an hour later, sugar 1·83 per cent.; 24 hours later, sugar 1·98 per cent. More sugar was therefore formed than the glycogen in the liver could possibly account for. But **Boehm** and **Hoffmann** object to this conclusion, on the ground that something other than sugar was reckoned as such.

The *hepatic cells* are devoid of all cell walls and possess one or two nuclei. As constituents of the dead cells we find an albumen coagulating at 45°; nucleo-albumen (**Plósz**), soluble in water and in solutions of sodic chloride and sulphate, and coagulating at 70°; an albumen resembling myosin, coagulating at 75°; free nuclein and a body resembling coagulated albumen; glycogen, grape sugar, and a diastatic ferment; fats, particularly olein, about 2·5 per cent.; pigments, potassic and sodic phosphates, and water.

To prepare glycogen and liver ferment, and to demonstrate sugar in the liver, see pp. 69, 149, 72. For *bile*, etc., also see p. 173.

Pathology.

	BIBRA.		FOLWARCZNY.		FRERICHS.		OIDTMANN.
	Fatty liver in tubercle	Typhoid liver.	In diabetes.	In embolism of the hepatic artery.	Fatty liver.	Cirrhotic liver.	Syphilitic liver in a new-born child.
Water	71·0	75·1	75·3	80·7	73·0	80·2	82·5
Soluble albuminoids	1·3	2·6	6·7	2·1	3·6	3·5	16·5
Gelatin	4·4	4·0	1·1	1·1	1·9	11·5	
Extractives . . .	2·6	4·5	2·2	3·6			
Fats	17·4	3·3	1·9	2·4	17·2	2·2	
Insoluble tissues .	3·1	10·2	11·7	8·9	4·0	3·6	9·1
" salts . .	—		—	0·5	—	—	
Soluble " . .	—	—	0·9	0·4			

Fats.—While the normal liver contains only about 2 to 3·5 per cent. of fats (that of the cat normally about 7 per cent.), and 19·5 to 20·7 per cent. other solids, in acute atrophy of the liver the fats may rise to 7·6 per cent., and the other solids sink to 15·5 per cent., and in fatty liver the fat may be as high as 19·5 per cent., and the remaining solids 18·4 per cent. This increase may occur in diseases of the respiratory organs, as phthisis, etc., and as a result of chronic alcoholism, degeneration, etc.

The *glycogen* is greatly diminished in fevers, and in arsenical and phosphorus poisoning; it may be absent from fatty liver, and it is increased in diabetes.

Pigments apparently identical with hæmatin accumulate in the liver in malarial affections, and in yellow atrophy we may find crystals of bilirubin.

Urea is increased, together occasionally with *leucin*, *tyrosin*, *cystin*, etc., in acute yellow atrophy and carcinoma of the liver, in many zymotic diseases, acute rheumatism, pyæmia, malarious cachexias, syphilis, tuberculosis, some diseases of the spinal cord and heart, chronic pleurisy, and in many cases of anæmia and jaundice. *Leucin*, it may be remarked, increases in the liver after death, and especially during putrefaction.

Concretions are met with now and again in the substance of the liver. They generally consist of organic matter 35 to 40 per cent., with calcic phosphate and carbonate about 32 per cent.

CHAPTER XXV.

THE PANCREAS.

The fresh human pancreas is alkaline in reaction and contains 17·4 to 25·5 per cent. solids and 74·5 to 82·6 per cent. water. Of the solids there are serum albumen, an alkali albuminate like casein, fats and volatile fatty acids, extractives, and salts. Among the extractives present are guanin (0·12 per cent.), xanthin (0·0016 per cent.), leucin (1·7 per cent.), inosit, butalanin, lactic acid, and traces of uric acid and tyrosin. No mucin is contained in it.

For *pancreatic juice* see p. 167.

Pathology.—The pancreas may be the seat of tumors (cancer, adenoma, etc.) or of infiltrations and degenerations. Very often, in such cases, the properties of its secretion are altered, and accordingly some of the intestinal contents may escape digestion, and this has been noticed chiefly in the case of the fats.

CHAPTER XXVI.

SPLEEN.

This organ is provided with an elastic capsule containing muscle-fibre cells, which is prolonged inwards on the blood vessels at the hilus of the organ. Enclosed by this capsule is the splenic pulp, that is supported by a coarse trabecular framework as well as by a delicate meshwork forming a honeycomb of membranes in connection with the vessels (Klein). The red pulp itself is made up of cells of different kinds and of blood corpuscles, particularly the pale ones, in different stages of change. Here and there are to be seen little spots of white pulp, the Malpighian corpuscles, which consist of small clumps of lymphoid infiltration in the sheath of the small arteries.

Functions.—It is possible that besides destroying old blood corpuscles it assists in forming new ones, the pale corpuscles especially; and it is said to prepare the proteolytic pancreatic ferment (Schiff), though this is denied (Mosler). It acts also as a regulator of the blood contents of the liver and stomach.

Chemical Composition.—In the fresh state the spleen is alkaline, but it becomes acid some time after death. The composition of the pulp may be thus stated (*after* Oidtmann, etc.):—

Human Spleen.	Per cent.		
Water	70	to	77
Organic matter	23	"	30
Inorganic constituents	0·5	"	0·9
" " in the 100 parts—			
Soda	35	"	45
Potash	9	"	17
Lime	7		
Phosphoric acid	18	"	30
Oxide of iron	7	"	16
Chlorine	0·5	"	1·3
Sulphuric acid	1·5	"	2·5
Silica	0·2	"	0·7
Manganese, copper, and lead	traces.		

There is some difference of opinion as to the occurrence of free iron in the spleen, but that iron is present in large excess, associated in some way with an alkali albumen, there seems to be no doubt; it appears also to increase with age, and of combined iron NASSE has found 5 per cent. in the dried pulp of the spleen of old horses.

The *organic constituents* include albumens, much inosit, cholesterin, cerebrin, xanthin, hypoxanthin, traces of leucin, uric, succinic, and lactic acids, fats, and iron-holding pigments. Tyrosin is a *post-mortem* constituent, and the volatile fatty acids, such as formic, acetic and butyric, are decomposition products, probably of the hæmoglobin products of the red pulp.

In its composition the splenic pulp differs from blood in the large amount of its soda and phosphates, and in the smaller proportion of its potash and chlorides, and it is characterized by its richness in extractives and pigments. Uric acid is always present, and seems to be connected in some way with splenic activity, particularly under abnormal conditions, as seen in ague, etc., when an increase in the uric acid in the urine accompanies an enlargement of the spleen.

Pathology.—In diabetes no *glycogen* is present, but a little sugar is to be met with; *xanthin* has been found in hypertrophy. In leukæmia the spleen is rich in *sarkin*, *uric acid*, *and bodies allied to gelatin*. ROBIN, CHARCOT, and NEUMANN have found peculiar crystals in the spleen in leukæmia. These crystals have been regarded as of the nature of tyrosin, but this has been denied. SCHREINER describes them as consisting of a phosphate of a base having the composition C_2H_5N; and he states that he has found a similar body in the human semen to the extent of 5·23 per cent. These crystals are met with also in the sputum of bronchitis, and in the blood and marrow in leukæmia. They are of a double pyramidal shape, and are insoluble in alcohol, ether, chloroform, and cold water, but soluble in alkalies and dilute mineral acids, acetic acid, etc.

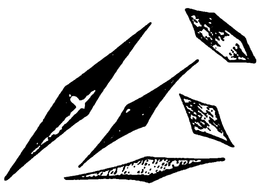


FIG. 26.—CHARCOT-NEUMANN CRYSTALS.

Amyloid degeneration is frequent in the organ.

CHAPTER XXVII.

SUPRARENAL CAPSULES, THYMUS, THYROID, LYMPHATIC GLANDS, AND KIDNEYS.

I. SUPRARENAL CAPSULE.—The medulla of this body has been considered nervous in its nature on account of its richness in nerve elements, while the cortex is glandular, somewhat of the character of lymphoid tissue. In the medulla together with albuminous bodies there is found a material that is soluble in water, and, particularly when exposed to the direct sunlight, furnishes a beautiful red pigment. The colorless extract is reddened by the action of watery solutions of chlorine, bromine, or iodine, and is stained of a dark blue to a green by perchloride of iron. Alcohol extracts this chromogen, and the solution gives a reddish precipitate with acetate of lead, which turns green on exposure to the air. A very dilute hydrochloric acid extract of the gland is colored red on the addition of excess of ammonia, violet flocculi being precipitated. Leucin, inosit, hypoxanthin, hippuric acid, benzoic acid, myelin, fats, and possibly taurin and taurocholic acid are all said to be present.

Among the *inorganic constituents* we find potassic chloride in large amount, also phosphates of potassium, sodium, calcium, and magnesium. This excess of potash and phosphoric acid speaks in favor of the nervous nature of the organ.

The juice of the gland is neutral or weakly acid. The proportions are thus given by OIDTMANN in the suprarenal of the dog:—

Water	80·03
Organic matter	19·88
Inorganic "	0·09

In ADDISON'S disease it has been found degenerated.

II. **THYMUS.**—This gland atrophies towards puberty, after having undergone fatty degeneration. It consists in great part of a sort of lymphoid tissue supported by fibrillated connective tissue.

Chemical Composition.—

In a Calf of 3 *Months* (SIMON).

Water	77
Albuminoid material	4
Salts	2
Fats	traces.

In a Puppy (OIDTMANN).

Water	80·7
Organic matter	19·2
Inorganic "	0·2

The chief solids are the following: soluble albumen, gelatin, fat, and elasticin; leucin, xanthin, hypoxanthin, succinic, lactic, and traces of other fatty acids; salts rich in phosphoric acid, potash, and soda; but, except in the very early period of the gland, potassium replaces sodium, being about three times more abundant; traces of salts of lime, magnesia, and ammonia, and of sulphuric acid and chlorine are likewise met with.

In the thymus of a calf, three weeks old, there was found only 1·3 per cent. fat, while in that of a young heifer of 18 months as much as 16·8 per cent. was present.

III. **THYROID.**—This organ is made up of connective tissue, scattered through which are a great number of different-sized cavities, more or less globular in shape; these are filled with a transparent fluid

John J. K[illegible] 9/7. 85

that is analogous to mucus; there is present in this fluid a little albumen and traces of sodic chloride and oxalate of lime, etc. The juice of the gland also contains leucin, xanthin, hypoxanthin, volatile fatty acids, succinic and lactic acids, and cholesterin. In the small cysts little or no albumen, is present, but in the larger cysts as much as 7 to 8 per cent. may be found. This fluid material of the cysts is very liable to undergo colloid degeneration, and in goitre it is produced in great excess, cholesterin crystals also being frequently abundant and occasionally crystals of bilirubin.

An alcoholic solution of chinolin blue stains this colloidal material of an intense blue.

OIDTMANN gives the subjoined as the general percentage composition of the gland:—

	In a child.	In an aged female.
Water	77·2	82·2
Organic matter	22·3	17·6
Mineral salts	0·5	0·9

IV. **LYMPHATIC GLANDS** contain about one-third their weight of solids, among which have been found nuclein, lecithin, albumen, cholesterin, leucin (but no tyrosin), xanthin, etc.

V. **KIDNEYS.**—The capsule is white fibrous tissue, and a certain amount of connective tissue is also found supporting the tubes.

The renal tissue has a mean density of 1050; its reaction is alkaline, but it speedily becomes acid when exposed to the air.

	Child's kidney (æt. 14 days).	Kidney of an old woman.
Water	77·82	81·09
Organic substances	21·47	17·92
Inorganic "	0·71	0·10 (OIDTMANN).

A *cold watery extract* of the kidneys contains albumen, xanthin, hypoxanthin, kreatin, taurin, leucin, inosit, cystin, glycogen, and occasionally also urea, uric acid, and urates. If a solution of subacetate of lead is added to it, the resulting precipitate suspended in water, decomposed there with sulphuretted hydrogen, and alcohol added to the filtrate, which is then gently warmed, a crystalline precipitate of *inosit*, *cystin*, *taurin*, *xanthin*, *and sarkin* is obtained. By warming this deposit with carbonate of soda solution we obtain on filtration a solution of cystin and inosit, from which the cystin can be precipitated by the addition of acid.

Kidneys thoroughly washed out with sodic chloride solution (¾ per cent.), to get rid of the blood, gave in the 100 parts the following organic constituents (GOTTWALT):—

Serum albumen	a mean of	1·25
Globulin substances	"	3·818
Albumen extracted by common salt solution (10 per cent.)	"	5·23
Albumen soluble in and extracted by sodic carbonate	"	1·52
Gelatin	"	1·016
Mucin	traces.	

Bunge and **Schmiedeberg** are of opinion that hippuric acid has its seat of formation in the kidneys, the glycocin and benzoic acid residues being combined under their agency, the presence of blood corpuscles, however, appearing to be essential.

Pathology.—In consequence of inflammations of different kinds, and as the result of the altered blood in phosphorus poisoning, excessive alcoholic ingestion, septicæmia, and severe eruptive fevers, the renal epithelium may become charged with granulations of the nature of casein; while a long continuance of one of the above conditions may further lead to the appearance of fatty granules, which possibly replace and are derived from the albumen granules, and thus lead to a subsequent *fatty degeneration*.

In some cases purulent abscesses may appear among the tubes, or excess of leucocytes.

In gouty conditions deposits of urate of soda frequently present themselves, and different morbid growths at times attack the renal substance.

In various abnormal conditions bodies may be present that are only rarely to be met with normally, and then in but slight amount: thus leucin and tyrosin have been found in cholera; uric acid in tuberculosis, delirium tremens, and Bright's disease; and grape sugar in diabetes mellitus.

A calcareous degeneration of the cortex of the kidneys has been noted in acute mercurial poisoning (**Salkowski**), and it would appear that this calcification of the renal tubules accompanies a removal of lime salts from the bones.

CHAPTER XXVIII.

THE LUNGS.

Owing to the large amount of elastic tissue, smooth muscle, connective tissue, cartilage, and epithelium present in the lung, the chemical constituents of these tissues will figure largely in the chemical composition of the lung, and accordingly we have much elasticin, mucin, myosin, chondrin, and gelatin; there is also casein, lecithin, leucin, inosit, and in the lungs of oxen taurin: further we have uric acid; inorganic salts, chiefly chlorides, sulphates, and phosphates of sodium, potassium, calcium, magnesium, and iron; and silica.

Lung substance contains more coagulable proteids than muscle, and less albuminoid extractives. The embryonic lung is rich in glycogen; in the embryo of the sheep it has been found as high as 50 per cent. of the dry solids; but it is wanting in the lungs of adults.

In the fresh state the reaction of the lung tissue is alkaline. Of *ash* in the dry solids there is found 2 to 7 per cent., chiefly alkaline phosphates, sodium chloride, and iron. The richness of the ash in phosphoric acid is due probably to the lecithin present.

Lung of Infant (**Oidtmann**).

Water	79·6 per cent.
Organic matter	19·8 "
Mineral "	0·6 "

Verdeil has described a special acid, *pneumonic*, which he has isolated (taurin?). A black pigment consisting chiefly of carbon (85 per cent.), with a little nitrogen, hydrogen, and ash, is present in the lung substance.

Pathology.—The lung may contain *tubercle*, which will present different appearances according to its condition.

Caseous Tubercle (Simon).

	Per cent.
Water	82·6
Insoluble organic matter	12·0
Substances soluble in alcohol	2·1
Fatty bodies, cholesterin, cerebrin, etc.	1·86
Watery extract	0·84
Mineral salts	0·49

Calcareous Concretions are often present in these tubercular deposits; they vary in composition.

Insoluble salts	70·1 per cent.	
Soluble "	29·5 "	(Boudet).

The soluble salts consist chiefly of sodium chloride mixed with phosphate and sulphate of soda; the insoluble salts, chiefly of phosphate of lime with a little carbonate, silica, and oxide of iron. They sometimes also contain cholesterin and a little proteid substance.

Concretions are also occasionally found in the lung tissue, as well as in the nose, tonsils, and tracheæ, etc.; they consist of mucin, fat, phosphate and carbonate of lime, and magnesia. They may contain 86·9 per cent. of inorganic salts, chiefly phosphate and carbonate of lime with traces of iron (Biermer); or consist of 70·1 per cent. of soluble salts (sodic chloride, phosphate, and sulphate) and 29·5 per cent. of insoluble salts (calcic phosphate and carbonate, silica, etc.), as given above by Boudet.

A Lung Calculus (Sgarzy).

Fatty matters and cholesterin	15·6
Calcic phosphate and carbonate	3·9
Mucin and albumen	7·2
Magnesic carbonate	0·9
Silica	0·8
Water	1·2

In pneumonia the lung becomes hepatized, which is owing to the solidification of the blood derivatives poured out into the air cells. In this condition glycogen has been found in considerable quantity.

Melanic as well as other tumors occasionally show themselves in the lung tissue; and well-marked pigmentation of the lung may be produced by an accumulation of oxide of iron particles, as in siderosis; or of fine carbon particles, as in anthracosis.

In anæmia leucin and tyrosin are often present; in Bright's disease, urea, uric and oxalic acid, inosit, and occasionally ammoniacal salts; in diabetes, glycogen and glucose; and occasionally the same in purulent pneumonia; in tubercle, cholesterin; and in calcareous degeneration, much lime salts.

Sputa consist of the secretions of the mucous lining of the respiratory tract, occasionally mixed with saliva or nasal mucus. Normally there is very little secreted, while in different diseased conditions the quantity is generally considerable, but it is very changeable. As examples the sputa of a few pulmonary diseases will be given here.

Diseases.	Sputa in grams in the 24 hours.	Water.	Solids.	Organic constituents.	Mucin.	Albumen.	Fat.	Extractives.	Ash.
Bronchitis .	135	97·6 –98·3	1·7–2·3	1·17–1·7	0·69–1·2	—	—	0·48	0·53–0·64
Pneumonia .	74	90·09–93·6	6·3–9·01	5·5 –8·35	1·1 –1·28	3·09	0·02–0·82	2·8–3·95	0·66–0·77
Phthisis . .	124	94·5	5·5	4·7	1·8 –2·4	0·29–0·49	0·36–0·39	1·6–2·01	0·76–0·8

In pneumonia the *quantity* may vary from 26 to 122 grams in the 24 hours; of the rusty sputa, from 30 to 300 grams; and in the stage of resolution, from 250 to 300 grams. In phthisis it may range between 80 and 150 grams, but the daily quantity is variable, much more so than is the case in bronchitis.

The sputa in different pulmonary affections vary greatly in color, odor, viscidity, thickness, etc. In consequence of chronic inflammation of the bronchi, especially when the air breathed is rich in particles of carbon, as with miners, etc., the expectoration may be quite *black; red*, from the presence of blood or blood pigment; or *green*, from biliary pigment. A putrid odor is given off by the sputum in cases of gangrene of the lung and bronchiectasis. As to *salts*, a large proportion of alkaline chlorides and phosphates, with a small proportion of sulphates, is usually present.

In an acute catarrh the mucus had this composition:—

Water	97·9
Solids	2·1
Organic	1·36
Mineral	0·63

But if the irritation is long-continued or excessive pus also may make its appearance. In old-standing bronchitis there are comparatively few cell elements in the expectoration, and, as we have seen in the table, little or no albumen or fat; but in acute bronchitis, acute congestion, and occasionally in hydro-pneumothorax, the albumen is much increased. In pneumonic sputa the amount of fat is small, but that of the extractives abundant, and the same holds good in phthisis. In tubercular phthisis the sputum may contain tubercle corpuscles and débris of different kinds; blood may also appear in such cases as well as in pneumonia, and it may be so abundant as to be readily recognized, or it may be so slight as to be masked. In case of doubt examine for blood by the hæmin and spectroscopic tests.

Pneumonic sputum in the *early stage* of the disease is brown or yellowish red, viscid, and somewhat translucent, consisting of a mixture of mucus, reddish serum with blood corpuscles, epithelial cells, and threads of fibrin, together with coagulable albumen. When the lung is *hepatized* the color of the sputum is less marked, but it becomes more viscid, and it may be grayish or purulent, and contain an excess of sodic chloride. The amount of this last salt is very considerable. In a case of pneumonia of the sixth day its proportion to the litre of sputum was equal to 4·5 grams, only 0·5 gram appearing in the urine of the 24 hours in the same time, while on the 13th day of the same case the proportion was equal to 8·20 grams per litre, and in the day's urine to 2·52 grams.

According to NASSE, 1 litre of laryngo-bronchitic mucus contains 5·8 grams of alkaline chlorides.

In *gray hepatization* the sputum becomes brown, less viscid, and presents grayish streaks; it is rich in albumen, and contains also mucus and pus corpuscles, fatty granules, and epithelial cells.

It should be remembered that the coloring matters of prunes, rhubarb, etc., may communicate a reddish tint to the sputum.

CHAPTER XXIX.

RESPIRATION.

Respiration is essentially a chemical phenomenon in which oxygen is absorbed, and carbonic acid and water exhaled at the lungs, the two latter compounds resulting from oxidations that have occurred in the tissues.

Changes effected upon the Air by Respiration.—The air in its passage through the lungs undergoes several changes.

1. The inspired air loses 4·7 per cent. oxygen, and the expired air gains 4·3 per cent. carbonic acid gas (Vierordt).

2. The expired air is saturated with aqueous vapor.

3. The temperature of the inspired air, if somewhat lower than that of the body, is raised to 33° to 36°, the exact temperature, however, depending on that of the air, and on the depth and rate of the respirations; but if the temperature of the inspired air is very low, then it will not be so high—*i. e.* temperature of inspired air 6·3°, temperature of expired air 29·8° (Valentin).

4. The volume of the expired air is slightly less (from $\frac{1}{50}$ to $\frac{1}{130}$) than that of the inspired air, while the volume of carbonic acid gas added to the air is nearly equivalent to that of the oxygen absorbed, the carbonic acid containing its own volume of oxygen; yet a little of the oxygen inspired does not thus reappear in the carbonic acid of the expired air.

5. The expired air is also said to contain traces of ammonia, hydrogen, carburetted hydrogen, and other hydrocarbons; perhaps also a slight trace of nitrogen in excess of that inspired, and very slight traces of organic bodies badly known. Some of these bodies probably arise in the intestinal organic decompositions (Pettenkofer). As to *ammonia*, young individual produce more than old, and small proportionately more than large animals. For every 100 lbs. body weight an adult man expires in the twenty-four hours about 3·9 grains, and a young boy about 6·2 grains ammonia (Grouven). According to Lossen, however, the average in the twenty-four hours for an adult is 0·014 gram (0·22 grain).

The amount of *free nitrogen* in the system depends greatly on the atmospheric pressure: if this is lowered nitrogen leaves the body; so also if the temperature is raised. In a state of hunger some nitrogen appears to be absorbed, while with well-nourished beasts a little seems to be exhaled from the organism. Pettenkofer and Voit, however, deny that free nitrogen is eliminated from the body to the extent asserted by Seegen and Nowak.

The *oxygen of the inspired air* traverses by effusion the fine membrane separating it from the blood, and it is then taken up in great part by the hæmoglobin of the corpuscles, with which it forms an unstable combination; a small portion is also dissolved in the liquor sanguinis.

Of the *carbonic acid exhaled* for every five parts only one part comes from the corpuscles, and the remaining four from the plasma.

(1) The portion in the corpuscles is probably combined with the hæmoglobin; (2) that in the plasma is partly in a state of simple solution, while the rest (3) is feebly combined with the sodic carbonate and phosphate of the serum (ZUNTZ). One chemical equivalent of common phosphate of soda enters into a loose combination with the same quantity of carbonic acid as two equivalents of carbonate of soda (FERNET). This loosely combined carbonic acid is readily evolved by reduction of pressure or the passage of another gas, especially in presence of albuminous bodies (SERTOLI) or in that of the colored corpuscles (PREYER). The oxyhæmoglobin which is formed in abundance early in the respiratory act would thus appear to form the part of an acid in liberating the combined carbonic acid. Indeed, according to HOLMGREN, the presence of oxygen in the lungs greatly increases the tension of the carbonic acid in the blood.

Other circumstances also assist; thus the rapidity of the blood current, and the great extent and moist condition of the respiratory surface, no doubt facilitate the diffusion and exhalation of the carbonic anhydride. Possibly also the diminished pressure in the air cells may assist in the elimination; and that some reduction of pressure in the interior of the lungs is possible we know to be the case. After DONDERS this is a normal occurrence, in some animals to the extent of —3 mm. and in man —1 mm. mercury, and in a forced inspiration to as much as —57 mm. But as to the exact *rationale* of the expulsion of the carbonic acid gas, our present knowledge is insufficient to enable us to say; and it is accordingly possible that other agencies are at work than we are yet acquainted with; indeed, none of the hypotheses that have been given hitherto can be regarded as perfectly satisfactory.

While the solubility of the *nitrogen* in the serum is regarded as the same as that of the gas in an aqueous solution of the salts of that fluid (FERNET, etc.), some consider the coefficient of solubility to be higher, the corpuscles possibly uniting feebly with a small quantity of the nitrogen (SETSCHENOW). As to the absorption of nitrogen in respiration nothing decisive can yet be said, but if it does occur at all it must only be in very small amount.

For every 100 vols. air inspired only 99·25 are expired, if calculated as dry air at the same temperature and pressure. This, as we have seen, is due to part of the oxygen absorbed not being replaced by carbonic acid gas. As a general rule, for every 100 parts of oxygen which disappear in the lungs, only 86 reappear in the carbonic acid gas, and nine or ten or more in the water exhaled. An adult man absorbs in an hour 28 to 36 grams oxygen, and he exhales in the same time 31 to 41 grams carbonic anhydride, corresponding to 22·5 to 30 grams of oxygen and 8·5 to 11·2 grams of carbon. The 5·5 to 6 grams of oxygen that have thus been retained in the organism are used up there in the different oxidations of the economy. One of these products is water, of which more is excreted than is absorbed. The extractives, including urea, etc., also carry away with them part of this retained oxygen.

Quantity of Air, Carbonic Anhydride, and Water Inspired and Expired.—1. After the most complete expiration 1,200 to 1,600 c.c. (73 to 97 cubic inches) of ***residual air*** remain in the lungs, or according to GRÉHANT 1,700 c.c. (104 cubic inches).

2. After an ordinary expiration there remain 2,500 to 3,400 c.c.—that is, from 1,300 to 1,700 c.c. (79 to 104 cubic inches)—of ***supplemental*** air.

3. The air taken in and expelled in each ordinary respiration—the so-called ***tidal air***—forms $\frac{1}{7}$ to $\frac{1}{10}$ of the vital capacity, or about 500 c.c. (30 cubic inches); it varies with age and size, etc., and may only amount to 330 c.c. (20 cubic inches).

4. The term *complemental* is applied to the quantity that can be inhaled after the deepest possible inspiratory effort beyond that introduced by an ordinary inspiration; it averages 100 cubic inches.

5. The ***vital capacity***, as it was termed by HUTCHINSON, is the amount of air expelled by a forced expiration after a forced inspiration. It varies from 200 to 300 cubic inches, being influenced chiefly by the height and weight, 8 additional cubic inches accompanying every inch of stature from 5 to 6 feet; corpulence and old age, on the other hand, causing a diminution in its amount.

The number of inspirations in a minute average from 16 to 19.

The ***total air respired*** in the twenty-four hours equals about 11 cubic metres (330·5 cubic feet), or 458 litres per hour (13·7 cubic feet), about 700 grams (355 litres, or 625 pints) of oxygen being consumed in the twenty-four hours. An adult inspires about 7 litres (427 cubic inches, 12·3 pints) per minute, and expires in the same time about 320 c.c. (0·56 pint) carbonic anhydride, and in the twenty-four hours about 800 grams carbonic anhydride (406 litres, or 714$\frac{1}{2}$ pints).

DUMAS gives the carbon exhaled by the skin and lungs in the twenty-four hours as 8$\frac{1}{2}$ oz., and E. SMITH as 7·14 to 11·7 oz.

The water exhaled by the lungs in the twenty-four hours averages between 350 and 500 grams ($\frac{3}{5}$ to $\frac{4}{5}$ pint); but some authors state the amount as averaging somewhat less than this, or only 10 oz. The former estimate would give a mean of 0·05 gram in each litre of air expired, a quantity varying, however, with the state of the organism as to bodily heat, respiratory depth and rapidity, and of the atmosphere as to temperature, pressure, and hygrometric condition.

The accompanying table indicates the changes effected in the air by the respiratory exchanges, and also the proportion of the gases in the blood:—

In 100 volumes.	Atmospheric air (DUMAS).	Expired air. (BRUNNER and VALENTIN.)	Expired air. (SPECK.)	Blood gases (PFLÜGER).
	Per cent.	Per cent.	Per cent.	Per cent.
Oxygen . .	20·81	16·033	16·43 to 16·84	38·08
Nitrogen . .	79·19	79·557	79·48 " 79·55	3·09
Carbonic anhydride .	0·037 to 0·062	4·380	4·09 " 3·61	58·83

The aqueous vapor in the expired air is variable, depending on the temperature; it averages 1·4 per cent., but the air contains only about three-fourths as much as it can hold when saturated, and in winter the proportion present is greater than in summer, although it is capable in summer, on account of the higher temperature, of holding nearly three times the usual quantity present.

A trace of ammonia is often present in the air, and occasionally traces of other gases in the air of large towns.

Circumstances affecting the Respiratory Exchanges, particularly with reference to the Carbonic Anhydride.

1. *State of Rest or Activity.*—The greater the labor effected in a given time the greater is the consumption of oxygen, and the greater the elimination of carbonic anhydride; but the period of increased exhalation of carbonic anhydride dependent on muscular work is generally followed by a period of diminished exhalation (RANKE). As the result of observations made on dogs in a state of repose and in a state of tetanus, the amount of carbonic acid gas expired was noticed to be increased proportionally to the degree of muscular work, during the period of rest an accumulation of oxygen also occurring in the system (SCZELKOW and LUDWIG). Muscle work, therefore, occasions a proportionally rich excretion of carbonic anhydride and absorption of oxygen in a given time, the venous blood coming from the active muscle being richer in carbonic acid and poorer in oxygen than the blood flowing away from a muscle at rest. The frequency and depth of the respirations accordingly bear a relation to the amount of muscle work, this increased frequency lasting for some time after the work has ceased.

Muscle work also greatly increases the water exhaled, sometimes more than doubling it.

2. *Food.*—The oxygen absorbed is employed for the oxidation of albumen, fat, and carbohydrates. While most of their carbon is burnt up, appearing as carbonic acid, part is otherwise excreted in urea and uric acid, etc. The sulphur also of the albumen is oxidized to the state of sulphuric acid, and the hydrogen to the state of water. Fats, we know, are very rich in hydrogen, and accordingly much oxygen is used up in their oxidation; carbohydrates, on the other hand, are more easily oxidizable, as they contain in themselves sufficient oxygen to combine with the hydrogen present to form water.

Some carbonic acid is undoubtedly formed in the body as the result of fermentation and other similar processes. Part of this, by diffusion from the intestine, enters the blood and is discharged at the lungs.

The quantity of air respired and of carbonic anhydride exhaled has two maximum and two minimum periods in the 24 hours, corresponding to the two chief meals of the day, breakfast and dinner. Less of the gas is expired during fasting than after food, and it is largely increased by an albuminous diet. A diminution in the exhalation is said to occur after the ingestion of alcohol, tea, etc.

The building up of the carbonic acid, it must be remembered, is not a respiratory act, or at least only so to a slight extent; it really depends upon the living cells of the organism, which regulate the consumption of oxygen and the breaking down of tissue. The carbonic acid thus generated is conveyed to the lungs to be discharged. As to this consumption of oxygen in the economy, PFLÜGER is of opinion that each living cell regulates its own consumption, and is independent of the pressure, even when pure oxygen is respired the intensity of internal combustion remaining the same as with air.

Respiratory Exchanges in Healthy Men under Different Conditions (PETTENKOFER and VOIT).

	Oxygen absorbed, in grams.			Carbonic acid expired, in grams.			Water expired.		
	Day.	Night.	Total in 24 hours.	Day.	Night.	Total in 24 hours.	Day.	Night.	Total in 24 hours.
Without food — rest .	420	323	743	379	316	695	463	351	814
Without food — work .	922	150	1,072	930	257	1,187	1,425	852	1,777
Mixed diet — rest .	469	450	919	539	404	943	534	475	1,009
Mixed diet — work .	795	211	1,006	828	306	1,134	1,035	377	1,412
Albuminous diet — rest .	632	218	850	580	423	1,003	696	414	1,110
Albuminous diet — work .	566	310	876	596	442	1,038	644	568	1,207
Non-nitrogenous food —rest	523	285	808	508	331	839	566	359	925

3. *Influence of Hunger.*—The expired air is only half saturated with aqueous vapor (E. SMITH). While the absolute quantities of oxygen absorbed and carbonic acid exhaled diminish, their proportion to the body weight increases somewhat. Starving beasts are said to absorb nitrogen from the air (REGNAULT and REISET).

4. *Day and Night, Light and Darkness, and Sleep or Wakefulness.*—The elimination of carbonic acid is increased in the light and diminished in the dark. Animals, it is known, fatten more rapidly if kept in darkness. During the day the elimination of carbonic acid is greater than in the night, but during the night less oxygen is exhaled than is absorbed. The color of the light is said to produce a difference, but the results of observers differ, some affirming that the most active evolution of carbonic anhydride occurs with a yellow light (SELMI); others, with violet (BÉCHAND); and others again, with yellow and green (POTT). During the period of hibernation that occurs in some animals only a small amount of carbonic anhydride is exhaled. It is said also that during the same time these animals absorb and retain a certain amount of nitrogen, but a far greater amount of oxygen. During sleep the exhalation of carbonic anhydride is diminished and a slight amount of oxygen is absorbed and retained beyond what occurs during a period of wakefulness. Thus, comparing the respective exhalation of carbonic anhydride and absorption of oxygen during rest and labor for the day and night, we have—

	For 100 CO_2 exhaled.		For 100 oxygen absorbed.	
	Day.	Night.	Day.	Night.
Rest	58	48	33	67
Labor	69	31	31	69

(PETTENKOFER and VOIT).

5. *Sex, Age, etc.*—The respiration is more active in the male than the female; and between 20 and 30 is the period of greatest activity, but proportionally to the weight the activity is greatest in youth (POTT), relatively more oxygen being absorbed and carbonic acid gas excreted.

In the female the elimination of the carbonic acid increases up to puberty, remains more or less stationary up to the cessation of the menses, and then declines. Males generally, however, exhale more carbonic anhydride than females.

In pregnancy the carbonic anhydride exhaled is increased, but diminished during menstruation.

6. *Size and Weight.*—Starting at five feet, each increase in height of one inch augments the vital capacity of the lung by about nine cubic inches (eight

inches, **Hutchinson**), and the same applies to an increase in the circumference of the chest (**Arnold**). But it must be remembered that in the same class of animals the intensity of the respiratory process is greater in its smaller members (**Bert**).

Thin animals absorb in general in the same time more oxygen than fat animals of the same species.

7. *Mode of Respiration.*—The frequency of respiration increases the total carbonic anhydride expired, diminishing it relatively, however, to the amount of air inspired. Thus with six respirations in the minute 28·5 c.c. CO_2 are exhaled with each expiration, and 171 c.c. in the minute; while with 12 respirations a minute there are 20·5 c.c. CO_2 in each expiration, and a total of 216 c.c. in the minute (**Vierordt**).

With deep and slow inspirations also more of the gas is expired, and a 1 per cent. increase may thus easily be attained.

8. *The State of the Circulation.*—A rapid circulation increases the exhalation of carbonic anhydride, as seen in cases of excitement and fever.

9. *Cerebral Activity or Repose.*—Not only is the temperature of the active organ raised, but the carbonic acid gas exhaled is increased by mental work.

10. *Season and Temperature.*—

In 100 parts.	Consumed.		Evolved.			
	Food.	Oxygen.	Water by skin and lungs.	Carbonic anhydride.	Total excreta.	
					Urine and fæces.	Nasal secretion.
December . . .	72·2	27·8	33·8	32·3	33·2	0·7
July	75·4	24·6	36·1	28·8	34·7	0·4
	100		100			

(**Barrall**).

A lowering of the temperature augments the exhalation of carbonic acid. This is well seen in the next table of **Vierordt's**, giving the mean of a series of observations on a man; the numbers relate to a period of a minute:—

	At 8·5°	At 19·4°
The pulse	72·93	71·21
The respirations	12·16	11.57
Volume of air expired . . .	6,672 c.c.	6,106 c.c.
CO_2 expired	299·3 "	257·8 "
Percentage of CO_2 to air expired	4·28 "	4·0 "

The increase in the exhalation of CO_2 is accompanied by an increase in the absorption of oxygen, and the increased carbonic acid is due to the intensified oxidation processes necessary to maintain the bodily heat (**Theodor**, **Voit**).

With high temperatures, on the other hand, the exhalation of carbonic acid is diminished (**Erler**), either from injury to the blood corpuscles or from interference with the respiratory movements. But with cold-blooded animals the carbonic acid is increased up to a certain point, with a rise of temperature.

11. *Alterations of Pressure.*—Much diminution of the atmospheric pressure enfeebles the respiration as well as the general muscular and cardiac activity; the oxygen absorbed and carbonic anhydride exhaled are also much diminished, and at the same time the urea excreted is lessened. These effects of diminished pressure probably result from the enfeebled tension of the oxygen.

If, on the other hand, the pressure is much raised, a sensation of cold is experienced, while the carbonic anhydride exhaled and the oxygen absorbed are diminished. The effects are due to the increased tension of the oxygen. This excess of oxygen, as when compressed air is respired, acts deleteriously; when nearly double the normal proportion, or about 35 per cent., is present in the arterial blood, it acts as a poison, convulsions and death occurring, as also a lowering of the temperature, indicating a hindrance to the oxidation (BERT). Thus under a pressure of 20 atmospheres, corresponding to 4 atmospheres of oxygen, an animal dies of asphyxia and convulsions. The production of carbonic acid is likewise diminished. At a still higher pressure oxidation is much diminished or ceases entirely, just as under a high pressure phosphorus will not burn.

12. *Species.*—Birds consume the most oxygen. The relation of the oxygen expired in the carbonic acid to the oxygen inspired varies considerably also in the same animal with the nature of the food: thus a bird fed exclusively on vegetables and grain excretes more oxygen in the carbonic acid exhaled than is supplied by the air inspired in the same period, a proof that in these animals part of the carbonic acid may come directly from the breaking down of the food itself.

13. *Disease.*—In febrile conditions the temperature is raised, and accordingly is attended with an increased production of carbonic acid. In a case of inflammation in a guinea pig the following results were obtained:—

	Oxygen absorbed for each kilo. of body weight in c.c. at 0° and 760 mm. during 1 hour.	Carbonic acid produced for each kilo. of body weight in c.c. at 0° and 760 mm. during 1 hour.	Proportion of oxygen in the carbonic anhydride to that absorbed.	Temperature.		
				Of the air.	In the rectum of the animal.	
					C.	F.
Normal condition.	948·17	872·06	0·92	18·7°	37·1°	98·7°
Slight fever . .	1137·3	949·5	0·83	17·5°	38·5°	101·3°
High " . .	1242·6	1201·59	0·96	15·9°	39·7°	103·4°

The absorption of oxygen and the production of carbonic acid gas are thus both increased with the elevation of temperature, the respirations also being greatly increased in frequency. In febrile conditions there is likewise an increased production of urea and of abnormal quantities of organic bodies poor in nitrogen or devoid of it.

Extensive anæsthesia of the sensory nerves leads to diminished respiratory exchanges.

Variations in the Respired Air.—If the proportion of oxygen is not reduced below 17 per cent., different inert gases may be mixed with it without risk, but in a gaseous mixture of 15 per cent. oxygen and 85 per cent. nitrogen sparrows will die in less than an hour. The presence, however, of even a very feeble proportion of certain *toxic gases* is sufficient to render the air unfit for respiration. When carbonic acid is present in the proportion of 4·5 per cent. the mixture has an asphyxiating action, but when it rises to 10 per cent. the asphyxia is very rapid. Even the presence of 1 per cent. makes itself felt, and in stables, etc., horses and the like begin to show symptoms of suffocation when the air around them contains only 0·3 per cent. It is found that when the proportion rises above a certain amount it tends to be redissolved in the blood and to induce narcotism. Accordingly air containing much carbonic acid is unfit for respiration, owing to its inability to discharge the blood of the carbonic acid it contains. With an increasing proportion of the gas accumulating in the respired air, a point is soon reached at which the gaseous exchanges between the blood and the air in the air cells of the lungs either ceases so far as the carbonic acid is concerned, or takes place too slowly and imperfectly to keep the blood sufficiently pure to allow the continuance of the vital processes of the organism.

In an atmosphere containing 58·53 per cent. oxygen and 20·09 per cent. carbonic acid gas rabbits die rapidly, although the oxygen present is double its normal amount in the air.

But the dangers of a confined and vitiated atmosphere are due not only to the excess of carbonic acid, but also to the accumulation in it of other respiratory products from the lungs and skin. For the mere presence of 1 per cent. carbonic acid in the respired air has very little effect, but an atmosphere in which the carbonic acid has been raised to this proportion by respiration is highly detrimental. Indeed, air rendered so impure by respiration as to contain even 0·08 per cent. carbonic acid gas is decidedly unwholesome. In an hour a man will add about 1 per cent. of the gas to about 70 cubic feet of air; and if the proportion is kept down to 0·1 per cent. at least 700 cubic feet should be supplied to him every hour, or about 16,800 cubic feet in the 24 hours.

CHAPTER XXX.

PROSTATE, TESTICLE, OVARY, AND SEMEN.

I. **The Prostatic Secretion** is troubled and slimy, and with an alkaline or neutral reaction; it contains albumens in very small proportion (0·45 to 0·92 per cent.), and salts, chiefly sodic chloride (about 1 per cent.), also potash and sulphuric and phosphoric acids; of water there is about 98·5 per cent. But comparatively little, it must be confessed, is known as to the exact nature of this secretion. It probably serves to mix with and dilute the semen.

Prostatic calculi frequently occur. These have been found with the following composition:—

	Per cent.
Water	8·0
Organic substances (with 2 per cent. nitrogen)	15·8
Lime	37·64
Magnesia	2·38
Soda	1·76
Potash	0·5
Phosphoric acid	33·77
A trace of iron.	

II. **The Testicle.**—The watery extract of the fresh testicle has been found alkaline (SERTOLI) and acid (TRESKIN). TRESKIN obtained the following bodies in the testicle: globulin substances precipitated by a saturated solution of sodic chloride, kreatin, inosit, leucin, tyrosin, lecithin, cholesterin, fats, and the chloride of potassium and sodium. Serum albumen, alkali albuminate, and phosphoric acid are probably also present, and glycogen has been found as an inconstant element (SERTOLI).

In the testicle of salmon MIESCHER obtained 25 per cent. solids, of which 10·95 to 14·72 are soluble in ether; these ethereal extractives consist in the 100 parts of—

Lecithin	51·8 to 53·12
Cholesterin	13·0 " 15·76
Fat	31·18 " 33·88

The secretion of the testicles is the semen, which is a white, viscid fluid that is characterized by the presence in it of the spermatozoa, which exhibit marked movements while alive and active. This power of movement they retain for several days in the alkaline fluids of the body, but they soon lose it in acid fluids, or in water, alcohol, ether, chloroform, or strong alkalies. They have much power of resistance against different reagents and do not decompose readily.

Spermatozoa.—As their chief chemical components we find nuclein, which appears to form their exterior, contained therein being certain albuminous bodies. Over 4 per cent. of sulphur-containing bodies are also present, and a proportion of water of about 82 per cent.

In the *nuclein* obtained from the spermatozoa of the bull there is 16·4 per cent. nitrogen, together with 7·189 per cent. phosphorus, but no sulphur. MIESCHER gives it the formula $C_{29}H_{49}N_9P_3O_{22}$. While the nuclein obtained from spermatozoa is free from sulphur, the similarly named body extracted from the nuclei of pus corpuscles contains 1·85 to 2·13 per cent. of this element.

In addition to the above lecithin, cholesterin, and fat have also been found in semen.

The pure spermatozoa of the salmon have this composition:—

	Per cent.
Nuclein	48·68
Protamin—a base in combination with the nuclein	26·76
Albumens	10·32
Lecithin	7·47
Cholesterin	2·24
Fat	4·53

The ether extract of the spermatozoa of the bull contains 51·6 per cent. of lecithin, and in the dry spermatozoa there is present 1·18 per cent. of sulphur and 2·36 per cent. of phosphorus, while of ash, containing much phosphate, there is about 5·21 per cent. Crystals also of an albuminous character have been found in the semen, which appear to be of the same nature as CHARCOT'S crystals, that are obtained from the splenic pulp and leukæmic blood, etc. They can frequently be obtained by spreading out some semen on a piece of glass and allowing it to dry slowly. It is possible, however, that these crystals may really be derived from the prostatic secretion. According to BÖTTCHER they are soluble in water, but shrink up and become opaque and insoluble in boiling water; they are readily soluble in alkaline solutions, insoluble in alcohol, ether, and chloroform, and are colored brown by iodine.

To the body named *protamin* has been assigned the formula $C_9H_{20}N_5O_2.OH$. It enters into combination with platinic chloride, and unites with some of the mineral acids. An ammoniacal solution of nuclein gives with a solution of a protamin salt a granular precipitate of nuclein-protamin, which is insoluble in water and ammonia, but easily soluble in dilute acids.

A body named *spermatin* has been described as present; it is allied to alkali albumen and mucin, and to its presence the semen is said to owe its mucilaginous consistency.

III. **The Ovary.**—The capsule and framework of this gland, like that of the testicle, is fibrous, and yields gelatin when boiled. The fluid in a Graafian follicle contains paralbumin. From the corpora lutea a yellow pigment (*hæmolutein*) can be obtained by means of chloroform, and this extract gives a spectrum with two absorption bands—one well defined and close to F, between it and *b*; and a second faint band between F and G.

Cysts frequently form in the ovary. Their contents vary somewhat, but the fluid is generally turbid, more or less dark colored, and often thready, having a specific gravity of 1020 to 1040, and containing 0·7 to 0·9 per cent. albumen. After this cystic fluid has stood some time a moderate amount of sediment falls, consisting of columnar epithelium, nuclei, cell detritus, and often cholesterin crystals. When it is diluted with water a turbidity appears, and by the addition of alcohol a precipitate is obtained of Scherer's *paralbumin*, a body not completely coagulated by boiling or by the addition of acetic acid, thus differing from Hoppe Seyler's *paralbumin*, which is precipitated by acetic and carbonic acids.

Very thready fluids generally contain in addition alkali albumen, mucin, mucin peptone, and Eichwald's *colloid*, a transition form between mucin and its peptone. When boiled with dilute sulphuric acid this colloid furnishes an unfermentable body that can reduce cupric oxide. It is insoluble in water, acetic acid, alcohol, and ether, but soluble in the alkalies and in strong nitric acid; iodine stains it brown, and Millon's reagent gives it a brownish red tint.

In some few large cysts a thin fluid of comparatively low specific gravity is found, containing serum albumen and alkali albuminate, but no paralbumin, and in addition some mucin and peptones. Occasionally the cystic fluid may be clear, watery, and very poor in albumens.

The largest cysts are found in the broad ligament, and their fluid contents are generally bright, clear, and slightly opalescent, weakly alkaline, having a specific gravity of 1002 to 1007, containing little or no albumen, sulphates, or phosphates, and depositing no sediment. Such a fluid contains about 2·2 per cent. dry solids, of which organic constituents form 1·3 (albumen 0·95 per cent.) and ash about 0·94 per cent., chiefly sodic chloride with traces of sodic and calcic carbonates.

CHAPTER XXXI.

DEGENERATIONS.

The tissues and organs having already been considered in detail, certain degenerations to which they are occasionally subject will here be very briefly referred to.

They may be classified into *fatty*, *colloid*, *mucous*, *amyloid or lardaceous*, *pigmentary*, *and calcareous*. But it is often difficult, it may be said, to distinguish between a morbid infiltration and a degeneration in which the tissue elements are transformed.

I. **Fatty Degeneration** is generally produced when the circulation in a part becomes insufficient. Fatty granules accumulate in the corpuscular elements of the tissue, giving them first a granular appearance and then causing them to break down, the protoplasm in its decomposition giving origin to urea, cholesterin, and fatty bodies. In phosphorus poisoning somewhat similar effects are brought about in the heart and liver, etc., with an increased excretion of urea in the urine.

This direct change of a proteid body into fat has been proved experimentally by placing fragments of muscle or coagulated albumen in the serous cavities of living animals (WAGNER), and also by the direct putrefaction of fibrin (WURTZ).

The degeneration may be preceded by an infiltration, and in certain acute diseases with a high temperature the tissue elements, particularly the glandular and mucous epitheliums and muscle, are invaded by fine granulations of a proteid nature. If this condition is prolonged the albuminoid infiltration may gradually undergo a fatty degeneration.

II. **Colloidal Degeneration.**—In cells as well as in muscles (as the adductors of the thigh), after certain eruptive fevers, uræmia, etc., an accumulation of homogeneous refracting material may be often noted gradually replacing the normal tissue, first giving rise to a granular appearance and then to a vitreous aspect.

In the follicles of the thyroid a similar colloid degeneration is to be seen. When cells are subjected to this degeneration they swell up, and after a time lose their outlines; and in proportion as the degeneration proceeds the colloidal material loses its consistency, and becomes a trembling mass very rich in sodic chloride, and consisting chiefly of a non-albuminoid body that is precipitated by alcohol and tannic acid, colored red by Millon's reagent, and to which the name of *colloidin* has been given (GAUTIER), with the formula $C_6H_{15}NO_6$; it possesses the properties of an amide derivative of the proteids.

III. **Mucous Degeneration.**—Normally a small proportion of mucin is present in some of the tissues; if this amount is greatly exaggerated, and at the expense of the proper elements of the tissue, we have mucous degeneration. An accumulation of a similar body is found in certain tumors (myxomata, enchondromata, and sarcomata).

IV. **Amyloid Degeneration** is due to the accumulation of a pale, waxy-looking substance in the tissues of a part, causing their elements to swell up and their nuclei to atrophy, and after a time their different elements to fuse into irregular blocks. The organs most subject to this change are the liver, spleen, kidneys, suprarenal capsules, and the walls of blood vessels, etc., and it is produced most frequently in persons who have been subject to syphilis, tubercle, carcinoma, or long-standing purulent discharges.

The amyloid substance contains 15·5 per cent. nitrogen and 1·37 per cent. sulphur. All its reactions seem to show that it is a mixture of a series of bodies closely allied to albumen (GAUTIER), although it has long been regarded as a special form of albumen. (For its characters see p. 120.)

V. **Pigmentary Degeneration.**—The pigment is not always the same, but it is probably a derivative of hæmoglobin decomposition. An abundant formation of this pigment occurs in melanæmia, Addison's disease, and melanic cancer.

The pigment occurs in the form of small dark granulations. The name *melanin* has been given to it. It dissolves slowly in caustic potash, forming a brownish red solution, and corresponds in composition to the normal pigment of the eye.

The pigment may also occasionally show itself in the form of crystals of hæmatoidin. In the disease named *chromhydrosis* this pigment is eliminated with the sweat.

The following is an analysis of a melanotic tumor (EISELT and BOLZE):—

Albumen	3·28	Soluble pigment	2·0
Insoluble tissues	7·92	Salts	1·0
" pigment	3·36	Water	82·4

VI. **Calcareous Degeneration.**—As the result of irritation of different kinds, of general or local disturbances of nutrition, and of senile atrophy, etc., there may ensue an infiltration of mineral salts into many of the tissues, particularly into the coats of the blood vessels and into costal cartilages, giving rise to the appearance of calcification.

The deposit consists chiefly of carbonate of lime mixed with phosphate of lime and traces of salts of magnesia. The new formation contains no ossein and presents no ossific structure.

CHAPTER XXXII.

MILK.

Physical Characters.—Milk is an opaque whitish fluid, having an opalescent, bluish tint in thin layers, and a specific gravity varying between 1018 and 1045, or averaging between 1028 and 1034 (SIMON); it is a natural emulsion, consisting of little globules of fat invested with coatings of casein and suspended in a solution of albumen, milk sugar, and salts. The reaction of milk is variable, woman's milk and that of the herbivora being normally alkaline, but that of carnivora acid; with the milk of herbivora, however, it is often possible to obtain a double reaction, both acid and alkaline, owing to the presence of an acid sodic phosphate (H_2NaPO_4) and of an alkaline disodic phosphate (Na_2HPO_4). Milk becomes acid on standing, owing to the conversion of part of its sugar into lactic acid; and at the same time the fatty globules rise to the surface, forming a layer of cream, some of these globules possibly also being freed from their protein envelopes (MÜLLER).

The so-called *uterine milk* is a white or rosy-colored, creamy, alkaline fluid, having a density of 1033 to 1040, which is obtained by gentle compression of the placental cotyledons of ruminants. It quickly becomes acid and coagulates. Fatty particles, free nuclei and epithelial cells are present in it. This has been assigned as its composition in the case of the cow :—

Water	87·91	Albumen and cells	10·40
Solids	12·09	Albuminate	0·16
(Fat	1·23	Ash	0·37)

In most new-born mammals the mammæ may secrete a little strongly alkaline fluid during the first month, which contains about 96 per cent. water, 1·4 per cent. salts, 0·9 per cent. sugar, 0·55 per cent. casein, and 0·49 per cent. albumen.

Amount Secreted.—From the third to the sixth month of lactation a woman secretes each day about 2 to 2½ lbs. of milk; but the amount is very variable, and may be taken as an average of 1¾ pint daily. A good cow gives about four times its body weight of milk in the year, or about six to seven litres (ten to twelve pints each day).

Chemical Composition.—The milk contains dissolved and suspended constituents; the latter are the corpuscles or globules which consist of particles of butter enclosed in minute casein envelopes, $\frac{1}{2500}$ to $\frac{1}{5000}$ of an inch in diameter, though some of them may be as small as $\frac{1}{20000}$ (FLEISCHMANN).

For a few days after parturition colostrum corpuscles, which are accumulations of fatty particles of a pale yellow color, $\frac{1}{1200}$ to $\frac{1}{800}$ of an inch in diameter, are also present. A few epithelial cells may likewise be met with.

With regard to the existence of the casein envelopes as distinct membranes, it should be mentioned that some doubts have been expressed by several observers (ZAHN, etc.); but if the milk is first mixed with a little caustic potash, and then well shaken with ether, the fat will be dissolved up by the latter—indicating, at any rate, the existence of an albuminous envelope of some kind.

The casein, sugar, and fat are formed in the cells of the mammary gland, chiefly, no doubt, at the expense of the proteids, by a differentiation probably of the serum albumen. The secretion appears to bear a direct proportion to the production of chyme.

I. *Solids in a Pint of Milk.*

	Grams.
Nitrogenous constituents	23·9
Fatty "	22·7
Saccharine "	30.3
Salts	4.0

II. *Composition of the Milk of Different Animals* (after GORUP BESANEZ, LIEBERMANN, GAUTIER, etc.)

Constituents.	Woman.				Ass.	Cow.	Goat.	Sheep.	Mare.
				Colostrum					
Water	86·27	88·91	87·77	84·08	90·70	86·56	86·76	83·30	82·84
Solids	13·72	11·09	12·23	15·92	19·30	13·44	13·24	16·69	17·16
Casein	2·95	3·92	2·34	3·23	1·70	3·50	2·92	5·73	1·64
Albumen						0·58	1·31		
Butter	5·37	2·67	3·68	5·78	1·55	4·03	4·48	6·05	6·87
Milk sugar	5·13	4·36	5·55	6·51	5·80	4·60	3·91	3·96	8·65
Inorganic salts	0·22	0·14	0·23	0 35	0·50	0·73	0·62	0·68	

In the case of colostrum the deficiency is in the casein, there being an excess of the other albumens. In woman's milk the proteids may vary from 1·1 to 4·19 per cent.; in one analysis TOLMATSCHEFF obtained 1·28 per cent. casein and 0·34 per cent. albumen.

(α) III. *The Ash of Milk in 100 Parts.*

	Woman's milk (WILDENSTEIN).	Cow's milk.	
		(WEBER.)	(HAIDLEN.)
Sodium	4·21	6·38	8·27
Potassium	31·59	24·71	15·42
Chlorine	19·06	14·39	16·96
Calcium	18·78	17·31	56·52
Magnesium	0·87	1·90	
Phosphoric acid	19·00	29·13	
Sulphuric "	2·64	1·15	
Ferric oxide	0·10	0·33	0·62
Silica	trace	0·09	

The potash salts, it will thus be seen, exceed the soda salts, the inverse of which holds good in the serum of blood.

(β) (VERNOIS and BECQUEREL.)

Salts insoluble in water	77·5 per cent.	phosphate of lime, with traces of other salts	70·06
		carbonate of lime	6·9
" soluble "	22·5 "	sodic chloride	9·8
		" sulphate	7·4
		other salts	5·3

Of ash in cow's milk BUNGE obtained 0·8 per cent., of which 22·14 per cent. = K_2O. 24·75 per cent. = phosphoric acid. 21·3 per cent. = chlorine. 20·05 = CaO, 13·9 = Na_2O. 2·63 = MgO. and 0·04 = Fe_2O_3.

Human milk is therefore much richer than cow's milk in potash salts.

IV. *The Relative Value of Different Kinds of Milk.*

	Water.	Casein and albumen.	Butter.	Sugar and salts.
Mare's milk	91·15	1·03	1·27	6·12
Ass's "	89·01	3·57	1·85	5·57
Woman's "	87·24	2·88	3·68	5·78
Goat's "	86·85	3·79	4·34	3·78
Cow's "	84·28	4·35	6·47	4·34
Sheep's "	83·30	5·73	6·05	3·96

V. *Condensed Milk.*

(α)	Per cent.		
Water	29	to	24
Solids	71	"	76
Casein	16	"	18
Fats	9	"	13
Milk sugar	8	"	18
Cane "	27	"	29
Ash	2	"	2·5
Phosphoric acid	0·2	"	0·7

(β) *Swiss Condensed Milk*—without added sugar, but with added benzoic acid (Fleischmann).

Water	52·31	Lactose	17·43
Fat	13·09	Ash	2·78
Albumen	12·13	Benzoic acid	1·74

VI. *Gases of Milk* (Pflüger) (at 0° and 1 metre pressure).

	In 100 volumes of milk.	In 100 volumes of gas.
Carbonic anhydride	7·60	90·48
Oxygen	0·10	1·19
Nitrogen	0·70	8·33

The *constituents of milk*, therefore, are *proteids*, principally casein with a little serum albumen; *fats*, as olein, much palmitin, much less stearin, and about 2 per cent. of the total fats as triglycerides of butyric ($C_4H_8O_2$), caproic ($C_6H_{12}O_2$), caprylic ($C_8H_{16}O_2$), with traces of myristic ($C_{14}H_{28}O_2$) and arachidic ($C_{20}H_{40}O_2$) acids, some of these last probably not being present in fresh milk; *milk sugar* or *lactose*, which varies least in quantity; and *extractives and salts*, chiefly potassic phosphate and chloride, and calcic phosphate, with traces of cholesterin and lecithin and of a body resembling lutein. But analyses show that great variation exists in the composition of milk, as is well seen in the case of cow's milk (Borries).

Woman's milk contains 87 to 90 per cent. of water, in which we find casein, serum albumen, a body like lacto-protein (Millon, Liebermann), together with fats, milk sugar, extractives, and inorganic salts. The *lacto-protein* body is not precipitated by boiling, by acids, or mercuric chloride, but only by the acid nitrate of mercury. Hoppe Seyler regards it as a mixture of serum albumen and casein.

Nasse maintains that casein contains more loosely combined nitrogen than other animal albumens, Lubawin considering it closely allied to nuclein. According to Radenhausen, when human milk is shaken up with ether it loses its opacity, which is not the case with cow's milk, this latter requiring the previous addition of caustic soda to bring about the same result. He is further of opinion that the casein of human milk is not true casein, but rather an albumen. Traces of peptone were also found by him in human milk. The casein of woman's milk also is not so easily precipitated by acetic and carbonic acid as that of the cow, and it forms a gelatinous mass difficult to filter; sulphate of magnesia, however, precipitates it more readily and completely.

Cow's milk contains some extractives that are said to be wanting in woman's milk: among these are urea (0·015 per cent.) and traces of kreatin; also acetic acid (0·004 to 0·014 per cent.) and alcohol—800 c.c. ass's milk yielding 30 c.c. of a distillate containing 3·5 per cent. alcohol and 0·036 gram acetic acid (Béchamp). Two different caseins are likewise mentioned, one soluble and the other insoluble (Selmi), and a trace of gelatin is also described.

The *casein* is an acid body (Rochleder), which in the pure form is scarcely soluble in water, but in milk it is combined with a soluble alkali albuminate. Calcic phosphate also serves as a solvent medium for the casein of milk.

The relative proportions of casein and albumen in milk are (Makris) casein, 1·87 to 4·68 per cent.; albumen, 0·60 to 1·77 per cent. In addition to serum albumen another albumen is described as present, having the composition $C = 52{\cdot}9$, $H = 6{\cdot}7$, $N = 14{\cdot}4$; it is not precipitated when the milk is acidified with acetic acid and a current of carbonic acid gas passed through it, nor is it coagulated by boiling.

A considerable amount of nitrogenous matter, apart from the casein and albumen, is contained in milk (Hoppe Seyler); in human milk it varies between 0·3 and 0·5 per cent., and in cow's milk it is about 0·7 per cent.

Danilewski describes three albumens in the whey of milk, the chief one being identical with the stroma albumen of the milk globules; the second an albumen of albuminoid character, named orroprotein; and the third being peptone.

Milk sugar is one of the characteristic constituents of milk, and butter the most variable one.

Coagulation of Milk.—Milk, even when just drawn from the cow, contains living organisms derived from contact with the udder, the hands of the milker, or the vessel in which the milk is collected. These are *aërobia*, which take up oxygen from the air and produce diastases that coagulate the casein. If a few drops of indigo-carmin solution are added to new milk filling a stoppered bottle, the color soon disappears, but is restored again on exposing the milk to the air.

The coagulation which is due to a deposition of the casein may occur spontaneously when the milk turns sour, or after the addition of rennet or of vegetable or mineral acids to warm milk. Tannin, alcohol, the salts of the heavy metals, and many neutral salts of the alkalies produce the same result.

But Hammarsten affirms that a pure salt-free casein solution gives no permanent precipitate even when strongly acidified, and that also for its coagulation to be effected by rennet the presence of phosphate of lime is indispensable; further, that when it is coagulated by rennet two new albumens are formed, one being a cheesy body soluble with difficulty in water, and the other a whey albumen that is easily soluble.

The spontaneous coagulation takes place in one of two ways. It is generally preceded by the formation of lactic acid from the milk sugar by the lactic ferment, the action of which is destroyed by neutralization of the milk with a few drops of sodic carbonate and then boiling, or by the addition of borax. But spontaneous coagulation may set in without the milk turning sour; it is not then due to the lactic ferment, but to *aërobia*, acting as casein ferments and active producers of diastases. This coagulation is not always arrested by boiling, even after the addition of sodic bicarbonate. As these ferments are most active at 40° to 45°, if the milk can be heated to this point without coagulating the temperature may then be raised to 100°, when the ferments will be destroyed (Duclaux).

When milk is boiled and allowed to evaporate, a scum or pellicle of insoluble casein forms on its surface, which is renewed on its removal. Colostrums, sow's milk, and the milk of carnivora coagulate when heated.

The presence of small quantities of salts, such as sodic and potassic chloride and acetate, etc., prevents to a certain extent the precipitation of casein by acids; so it is possible that when acid is added to a pure solution of casein minute traces of salts may be generated by the action of the acid on the casein. The coagulation by acid is probably a precipitation of the casein by a neutralization of the solvent alkali; but for the acid to effect precipitation it must be added beyond the point of neutralization.

Milk that has been boiled coagulates spontaneously with difficulty, but after having been acidified it does so more readily than unboiled milk. Boiled milk is also more difficult to coagulate by rennet than fresh unboiled milk.

Fresh milk is not coagulated by boiling even after a current of carbonic acid has been passed through it, but if the milk has stood some time coagulation will be thus produced, while if a sufficient time has elapsed, and a sufficiency of lactic acid has been developed, boiling alone will effect the coagulation; later still a current of carbonic acid will coagulate the milk, and finally the milk will set of itself, the coagulum consisting of casein and fat, and the whey of a solution of milk sugar, lactic acid, and inorganic salts, with a little fat albumen, and traces of casein. Heat accelerates the process considerably.

Rennet, we have seen, causes milk to coagulate, and this occurs whether the milk is weakly acid or alkaline, and more rapidly at a moderately elevated temperature than at a low temperature; but it coagulates with difficulty if it has been previously heated to 75°. Milk as it comes from the cow has a temperature of 37°; the ordinary temperature at which coagulation occurs is 25° to 35°; at 65° the diastase of the rennet is destroyed, at 10° pure rennet may be left in contact with sterilized milk for an indefinite time without causing coagulation, and at 41° the maximum effect is produced. The addition of a 1 per cent. sodic chloride solution causes the curdling to be more rapid; the same occurs also with a dilute potash solution, whereas with a 4 to 10 per cent. sodic chloride solution it is rendered much slower.

An active rennet may be thus prepared: The stomach of a young calf is rapidly washed in plenty of cold water, then distended with air, and hung up in a dry place for two or three months. All the walls, except a small portion round the pylorus, are cut up into small pieces and macerated for two or three days in six times their weight of sodic chloride solution (5 per cent.); more of the same saline solution, or some 5 per cent. boric acid solution, is next added, the whole allowed to stand for some time, then decanted and filtered. The filtrate is to be preserved in the dark in full bottles tightly corked; or seven to eight times its volume of alcohol may be added to it, the precipitate filtered off after twelve hours, and dried at a gentle heat. This last keeps well and may be dissolved in water when required (DUCLAUX). One part of this dry mucus, which need not contain more than 10 per cent. diastase, will cause 200,000 parts of milk to coagulate in 45 minutes at 37°.

Free lactic acid liberates the casein from its alkali combination, and accordingly rennet acts more completely on a milk that has stood some time, in which part of the milk sugar has fermented; but the coagulation of the casein by rennet and by lactic acid are not to be regarded as identical. Milk, it may be said, contains a lactic acid ferment, or a body that is readily converted into it; it is precipitable by alcohol.

Alterations in Milk produced by Exposure to the Air, Age of the Animal, Character of the Food, etc.

(*a*) *Exposure to the Air.*—Milk exposed to the air absorbs in three days more than its own volume of oxygen, part of its casein being transformed at the same time into butter (HOPPE SEYLER); and by degrees the milk turns acid from the production of lactic acid at the expense of the sugar. When the lactic acid rises to 4 per cent. it ceases to increase. If the milk is frequently agitated in the air, alcoholic or even butyric fermentation may be set up. Boiling retards the acidification, and the same results from the addition of thymol and boracic acid or its glyceride.

(*b*) *Age and Habit.*—In women's milk comparatively little difference seems to exist between the ages of 20 and 35, although after 20 it is said to become somewhat thinner, containing more water and less casein and butter. Before the age of 20 the milk contains more salts, casein, and butter than later in life; and after æt. 35 it is a little poorer in salts, the other elements apparently remaining unaltered.

It has also been stated that women of spare habit secrete a milk richer in solids (as casein, etc.) than women of robust habit, and that the milk of brunettes is richer in casein, butter, and milk sugar than the milk of blondes (L'HÉRITIER); but no difference has been observed by others (TOLMATSCHEFF).

The milk of a mother after her first child is said to contain less solids than that secreted after subsequent confinements.

(*c*) *Duration of Secretion.*—Milk secreted by the mother the first three or four days after parturition contains an excess of fat and is named the *colostrum.* This is a slimy, yellowish, alkaline fluid, having a specific gravity of 1040 to 1060, which on standing separates into two layers; compared with ordinary milk it is richer in fat, milk sugar, and salts.

Shortly before parturition the human milk contains about 14 per cent. solids, about 2 per cent. butter, and 3½ per cent. sugar; but about 24 hours after delivery nearly 16 per cent. solids, which diminish about 1 per cent. every few days till the twelfth day, when they average about 9·5 per cent. Two days subsequently to parturition the butter averages nearly 5 per cent. and the sugar 6 per cent.—proportions that diminish rapidly to the normal (CLEMM, etc.)

During the first five months the salts are in excess, and then progressively decrease to the eighth month, when they increase slightly; the casein and extractives diminish up to the second month, and then remain nearly constant, but from the tenth to the twenty-fourth month the casein declines; from the eighth to the tenth month the sugar increases, this body being in small proportion during the latter part of the first month; and in the fifth and sixth, and tenth and eleventh months the butter falls in proportion, progressively diminishing from the first to the eighth month, and then increasing slightly.

After suckling is given up the solids rapidly fall. The milk secreted after a long period of lactation is generally poorer in casein and richer in other albumens than the milk secreted at an earlier period.

(*d*) *Influence of Frequent Removal of the Milk, Time of Day, Season, etc.*—The less frequently the milk is taken from the mammary gland the greater is its proportion of water, the last portions removed being generally the richest in butter, generally containing seven times more than the milk that comes away at first—due probably to the greater degree of agitation to which this last portion has been subjected, and possibly also to its coming from the finer canals.

In mammals it has been observed that the evening milk is nearly twice as rich in butter as the morning milk. If a cow is milked three times a day, the proportion especially of casein and of butter is higher in the evening, the salts remaining about the same (**Bödecker**):

	Morning.	Midday.	Evening.
Specific gravity . .	1038	1040	1036
Water	89·9	89·2	86·6
Solids	10·1	10·8	13·4
Casein	2·24	2·36	2·72
Sugar	4·30	4·72	4·19
Butter	2·17	2·63	5·42
Albumen	0·44	0·32	0·31
Ash	0·83	0·69	0·78

(Fleischmann.)

	Morning.	Evening.
Specific gravity	1031·6	1031·8
Percentage of fat	3·37	3·42
Yield for each cow in kilos . . .	3·552	3·439

According to **Erlenmeyer**, however, midday milk is the richest in fat, and morning milk the poorest, because of the greater quantity of milk that has been formed since the previous milking. **Fleischmann** states, as the result of observations continued over three years, that in morning milk the fat, dry solids, and specific gravity are lower than in evening milk, the difference being slight but constant.

In summer the milk is more abundant and richer in butter than in winter.

(*e*) *The Food.*—While the quality of the food does not seem to exercise much influence on the character of the milk, the quantity appears to do so (**Decaisne**). Yet, according to some authorities, a food rich in proteids increases the butter and sugar (**Subbotin, Weiske**). An exclusively animal diet increases the albumen at the expense of the casein. Abundance of food increases both casein and fat, while a lessened diet diminishes the total solids with the exception of the albumen.

(*f*) *Rest* seems to encourage the formation of butter, exercise impoverishing the milk in butter, but enriching it in casein. The *emotions* appear to exercise considerable influence on the character of the secretion. During *menstruation* the milk is richer in solids (**Roger**), but it appears to contain less nutritious principles and is more liable to excite gastric disturbance in the infant. Probably the chief chemical alteration consists in the diminished proportion of sugar.

BUTTER.—Cow's butter contains about 68 per cent. palmitin and stearin, 30 per cent. olein, and 2 per cent. special fats (**Bromeis**), and the solid fats appear to be more abundant in winter than in summer (**Braconnot**). But the standard proportion of fixed acids in genuine butter fat has been variously fixed by different chemists—87·5 per cent. (**Hehner**), 88 to 88·36 per cent. (**Bischoff**), 89·73 per cent. (**Fleischmann**).

The amount of fat in cream is also said to vary very much, from 14 to 44 per cent. (**Wanklyn**).

By mechanical agitation the butter can be separated from the milk globules. This is effected most readily at a temperature of about 14°, after the milk has become slightly acid, and when the strokes of the instrument used in producing the agitation do not exceed 30 to 40 in the minute. To this operation the word "*churning*" is applied.

About two-thirds of the milk fat can thus be obtained as butter, the other third remaining behind in the buttermilk. 100 kilos. (220 lbs.) of milk, furnishing a mean of 15·6 kilos. (34 lbs.) of cream, yield 3 to 4 kilos. (6·6 to 8·8 lbs.) of butter. The butter thus prepared may contain as much as 18 per cent. casein; it melts between 30° and 40°, and is readily soluble in alcohol and ether. By exposure to the air and direct sunlight butter becomes rancid, owing to the development of fatty acids, glycerin, acrolein, and formic acid, etc., making their appearance.

The peculiar smell and taste of rancid butter is generally assumed to be due to the presence of free butyric acid, but according to HAGEMANN this does not seem to be the case, being due more likely to the formation of lactic acid by a process of fermentation from the milk sugar contained in the butter.

The Preservation of Milk.—A number of different bodies like salicylic acid, ether, chloroform, phenol, borate of soda, and boroglyceride, when added in small proportion to milk, tend to preserve it; but this preservation is best effected by evaporating the milk to a thick syrup under a reduced pressure, and adding to it a considerable quantity of cane sugar; this on dilution gives a fluid corresponding to the original milk, except in containing more saccharine matter.

Digestibility of Casein.—Rennet precipitates casein in compact masses both from raw milk and milk that has been warmed a short time at 50° to 70°. If the milk is boiled or kept two hours at 70° (BECKER'S method of milk preservation) a fine flocculent curd soon forms with rennet. Digestion experiments with artificial gastric juice and subsequent colorimetric determination of the peptones show that BECKER'S preparation yields most peptones, boiled milk coming next, and raw milk yielding least.

Substitutes for woman's milk have been proposed for children.—If we compare woman's milk with that of the ass and cow we find—

	Woman.	Ass.	Cow.
Casein	2·7	1·7	4·2
Butter	3·5	1·3	3·8
Milk sugar	5·0	4·5	3·8
Salts	0·2	0·5	0·7

(FRANKLAND.)

Therefore the proportion of casein in cow's milk is too high and that of milk sugar too low. In the substitutes proposed an attempt is made to obviate this. But it should be remembered that the casein of woman's milk does not appear to be exactly identical with that of cow's milk.

I.	Unskimmed milk	600 grams.	
	Cream of milk	13 "	
	Crystallized sugar of milk	15 "	
	Phosphate of lime (recently precipitated)	1·5 "	
	Water	339·5 "	(COULIER.)

II.	Wheat flour	1 oz.
	Malt "	1 "
	Potash bicarbonate	14½ grains.
	Mix well and add	
	Water	2 oz.
	Cow's milk	10 "

Warm the mixture, with continuous stirring, over a very slow fire till it becomes thick, then remove from the fire and stir well for five minutes; put it on the fire again and take it off as soon as it gets thick; finally let it boil well. It should form a thin and sweet liquid previous to the last boiling. Before use strain through muslin.

III. Heat half a pint of skimmed milk to 35°, and add to it a little rennet; let it stand in a warm place, either over a lamp or in some hot water, for ten minutes or so. Break up the curd finely with a knife, and after a quarter of an hour strain the whey through muslin and boil it in a small saucepan, adding to it 110 grains of powdered sugar of milk. Strain again through muslin, and when quite cold add to it two-thirds of a pint of milk fresh from the cow, and two teaspoonfuls of cream, stirring well together. The milk obtained should be kept in a cool place; a little of it is warmed when required, but it must be freshly prepared every 12 hours (FRANKLAND).

Pathological Alterations in Milk. *Drugs, etc.*—Salts of iodine, antimony, and arsenic rapidly appear in the milk after their administration; also salts of mercury after heavy and repeated doses, though this is denied (KUHLER). Boric acid, chlorides, alkaline carbonates, and salts of iron, lead, and zinc may likewise appear; also the organic acids, morphia, and other alkaloids. The ingestion of certain poisonous plants and of damaged grain affects the milk injuriously.

In certain *morbid conditions* there is an increase of the albumen at the cost of the casein. In osteomalacia the lime salts are increased. Blue milk has been observed containing a colored *vibrio*. *Blood* and *pus* may be present. The contour of the globules may be altered and not sharply defined, and their number lessened (as in "distemper" of cows).

During *acute fevers* the secretion of milk decreases, the casein increasing, but the sugar and fats diminishing.

In *chronic diseases* the proportion of casein falls slightly, while the butter and salts increase, the sugar remaining constant.

In *tubercular consumption* it is said that the milk acquires a peculiar infective taint. In *syphilis* the salts are doubled, but the casein and butter are diminished. In different *cachexias* the nutritive qualities are lessened. In the *rinderpest* in cows the milk is often of a reddish yellow color; it may contain blood and possess a nasty taste; the proportion of butter and sugar may sink to one-third the normal, while the albumen and salts may be increased to three times their ordinary amount, the casein also being doubled. HUSSON found the following percentages: casein 5·02, albumen 2·06, fat 1·26 to 1·49, sugar 1·64 to 3·14, salts 1·85.

CHAPTER XXXIII.

THE ANALYSIS OF MILK.

Physical Characters.—Good cow's milk is white with a faint yellowish tint, or when diluted it is bluish white; it has a fatty and not a watery feel between the fingers; if undiluted a drop of it placed on the thumb nail retains its shape instead of rapidly spreading out, which it is very likely to do if it has been diluted or if it proceeds from an unhealthy source. Its specific gravity should not be lower than 1018 or higher than 1045; an average of 1029 to 1033 at 15° is given by some authorities. The reaction is generally alkaline, though at times it is amphoteric, and occasionally while the first of a milking is alkaline the last of it may be acid.

TESTS.—I. Qualitative.

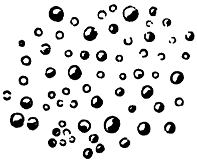


FIG. 27.—MILK GLOBULES.

1. Examine a drop *under the microscope* and note the globules; then add a drop of acetic acid, and on moving about the cover glass the globules will be seen to coalesce, owing to their casein coatings having been dissolved. In addition globules of free fat may be seen and large granular fatty cells (particularly in human milk after parturition), also fine free granulations consisting chiefly of casein and nuclein, and disappearing on the addition of caustic potash.

2. *Take the specific gravity.* As the hydrometer or lactometer is generally graduated for a temperature of 15°, the milk should be brought to this point if accurate results are required; otherwise a correction must be made. Normal cow's milk is said to indicate 1028 to 1034. Dilute some normal cow's milk with half its volume of water and take the specific gravity: it will vary from 1014 to 1016.

The following numbers have been given, but they are probably a little too high:

		With skimmed milk.		Unskimmed milk.							
A spec.	grav. of	1037	to 1033	or 1033	to 1029	indicates a pure milk.					
“	“	1033	“ 1029	“ 1029	“ 1026	“	milk	with	10	per cent.	water.
“	“	1029	“ 1026	“ 1026	“ 1023	“	“	“	20	“	“
“	“	1026	“ 1023	“ 1023	“ 1020	“	“	“	30	“	“
“	“	1023	“ 1020	“ 1020	“ 1017	“	“	“	40	“	“

3. *Separate the casein* by diluting the milk, acidifying slightly with acetic acid, and heating up to 60° or 70°; but by heating to 80° the flocculent precipitate becomes more marked, and a more complete separation of the casein is effected by subsequently passing a current of carbonic acid gas. The greater part of the butter separates with the casein. To detect it wash the casein precipitate with water, exhaust the washed mass with a mixture of alcohol and ether, and evaporate the extract thus obtained. Boil the filtrate from the first casein precipitate, or add to it potassic ferrocyanide, and a *precipitate of the serum albumen* will be obtained.

4. *To Separate the Butter.*—Add to a little milk contained in a long cylindrical tube half its volume of caustic potash solution (10 per cent.), and then shake the mixture rapidly with twice its volume of ether. Next insert the tube in a vessel containing hot water; the ethereal solution accumulates at the top of the fluid in the tube, and when it evaporates leaves a layer of butter behind.

Or take a long graduated tube closed at one end and fill it one-fourth with milk, one-fourth with ether, and another one-fourth with spirit (about 86 per cent.); cork it, and having shaken it well leave the tube inverted for some time at a temperature of about 40° until an oily layer has formed and appears not to increase. By this means a better estimate can be formed as to the amount of butter present.

5. *Separation of the Globules by Filtration and Detection of Albumen in the Clear Filtrate.*—By means of a reduced pressure filter milk through porcelain (p. 41); the globules will be stopped and a clear fluid will pass through containing albumen. Show this by testing the clear filtrate successively by boiling it and by the addition of nitric acid.

6. *To Detect the Sugar.*—Warm some milk, after the addition of a few drops of acetic or hydrochloric acid, to 40°; filter after some time through a moist plaited filter; shake the filtrate with ether, to separate the fat completely; then boil it to coagulate the dissolved albumen; filter, and evaporate the filtrate to a thick syrupy consistence, when the lactose will be gradually deposited in a crystalline form.

7. Tincture of guaiacum added to a drop of *fresh* milk in a watch glass produces an intense blue coloration at once or after a few seconds. Milk that has been boiled remains uncolored.

II. Quantitative.

1. *The Solids.*—(j) To 10 grams dry sand or powdered gypsum add 5 c.c. milk, then dry the mixture for a long time at 100° until the weight is constant. The increase in weight is equal to the solids in 5 c.c. milk. Suppose this to be = 0·5 gram, then 100 c.c. milk contain 10 grams, or 10 per cent. solids (BAUMHAUER).

Instead of 5 c.c. 10 grams of milk and 20 grams of dry sea sand may be weighed in a tared capsule of about 50 c.c. and evaporated at 100° till the weight is constant. When quite cold the capsule, with its contents, is weighed in a desiccator over sulphuric acid.

(ij) Place a little milk in a platinum capsule, and having weighed it, add a few drops of alcohol or acetic acid; evaporate over a water bath, dividing the coagulum against the sides of the dish, and dry it at 100° to 110° until the weight is constant. It is generally completed in six hours (GERBER). Cover carefully before weighing, as the residue is very hygroscopic.

The total solids should not, as a rule, be much less than 11·5 per cent.; cow's milk, for example, varies between 10·5 and 15 per cent.; less than this indicates dilution.

2. *The Butter.*—(j) Shake the milk well, and to 20 c.c. of it add 20 c.c. of a 10 per cent. caustic potash solution, and then some ether (60 to 100 c.c.), and agitate vigorously for some time; on standing the ethereal solution of the liberated fat rises to the surface, and is to be carefully decanted into a weighed porcelain dish. Some more ether is to be added to the alkaline milk, and after vigorous agitation it also is to be transferred as before to the capsule. The same process may be repeated several times if necessary. The ethereal extract is now evaporated over a water bath, and after having been dried in an air bath at 110° the weight of the residue is to be ascertained; this multiplied by 5 gives the percentage. With cow's milk it varies between 2 and 5 per cent., but the normal minimum for fats is about 2·75 (CAMERON).

(ij) An *approximative determination* may also be made by means of a graduated narrow glass cylinder or lactometer divided into 100 degrees from above downwards. The milk, well shaken, is poured into this vessel until it stands at 0°; the whole is then laid aside for 24 hours at a temperature of 10° to 12°. The cream rises to the surface and forms a layer, the thickness of which is to be read off at the end of this time. Good milk should yield from 10 to 15 per cent. of cream.

(iij) *Determination by the Optical Method.*—Both the following processes are founded on the determination of the degree of opacity of milk, which depends on the number of globules present.

(*a*) *With the galactoscope of* DONNÉ the light of a candle is examined in a dark room through a variable length of column of milk until the light is occluded, and from the length of column at which this occurs the richness of the milk in corpuscles is estimated.

(*b*) VOGEL'S *milk test* consists in the addition of small measured portions of milk to 100 c.c. of water, until a portion of the mixture transferred to a glass test vessel with parallel walls 0·5 c.m. apart renders it opaque to light. The percentage of fat is obtained by the formula $x = \frac{23 \cdot 2}{n} + 0 \cdot 23$, n being the number of c.c. of milk required to produce the opacity.

A cylindrical bottle is used in which to mix the milk and water. 100 c.c. of water is first placed in this bottle, and then by means of a finely graduated pipette 3 c.c. of milk added, and the two shaken together. The glass test vessel is then filled with the mixture and placed in a darkened room, about a metre in front of a stearin candle. If the image of the flame can be seen through the layer of liquid, then return it to the bottle and add 0·5 c.c more milk to it; shake the bottle and repeat the experiment. This is to be continued until the outlines of the flame can no longer be seen through the layer of fluid in the test vessel.

6 c.c. pure cow's milk forms a mixture with 100 c.c. water which completely obscures the flame of a candle in a darkened room. When more milk than this is required dilution with water is indicated: thus when 12 c.c. are needed 50 per cent. too much water is present in the milk, and when 8 c.c. about 30 per cent.

3. *The Casein and Albumen.*—j. (*a*) Dilute 20 c.c. milk with 400 c.c. of water and treat the mixture with very dilute acetic acid added *drop by drop until a flocculent precipitate begins to appear.* Now pass a current of carbonic acid gas through the fluid for 15 to 30 minutes, and lay aside for one or two days. Collect the precipitated casein on a weighed filter, wash it with spirit and then with ether until a drop of the washings leaves no fatty stain on paper; dry at 100° and weigh. Subtract the weight of the filter, and the difference multiplied by 5 gives the percentage of casein.

In the case of human milk precipitate the casein by saturating with magnesic sulphate.

(*b*) The filtrate from the casein precipitate is to be concentrated to a small bulk over a water bath, and an acetic acid tannin solution added so long as any precipitation occurs; and after the precipitate has settled collect it on a weighed filter, where it is to be washed with dilute spirit until the filtrate gives no blue coloration with ferric chloride (indicating absence of tannin); dry now at 100° and weigh. The weight multiplied by 5 gives the percentage of albumen.

In cow's milk the casein varies between 3·3 and 6 per cent., and the other albumens from 0·3 to 0·4 per cent. In diseased milk the casein may be as low as 0·2 per cent. and the other albumens as high as 10 per cent.

ij. (*a*) 10 c.c. milk is diluted with 100 c.c. distilled water and well mixed; a copper solution made by dissolving 63·5 grams cupric sulphate in 1 litre of water is then added slowly with stirring until the coagulum begins to settle quickly. The whole mixture, together with half the cupric sulphate solution already employed, is then added to some potash solution (50 grams potash to the litre), and after a short interval the clear fluid is filtered off through a filter dried at 110°; the precipitate is washed until the washings amount to 250 c.c., and the sugar is to be estimated in this subsequently.

(*b*) The coagulum on the filter is next treated with absolute alcohol, slowly dried, and extracted with ether; the ethereal and alcoholic extracts are then to be distilled, and the fatty residue dried and weighed. The coagulum, after having been dried at 125°, is weighed, then ignited, the ash deducted, and the difference taken as pure albuminoid (RITTHAUSEN).

4. *The Sugar.*—(j) Take 25 grams of milk, acidify with hydrochloric acid, boil, and filter, washing the coagulum with water; and to convert the milk sugar into glucose boil the filtrate and washings for an hour or so in a flask to the mouth of which a long tube has been attached. When the liquid cools make its volume up to 200 c.c., and determine the sugar by Fehling's method (p. 87), measuring 20 c.c. Fehling's solution into a flask, diluting with 80 c.c. water, and to the boiling mixture adding the diluted filtrate from a Mohr's burette until the copper is entirely reduced.

(ij) This sugar determination may be readily effected by the polariscope. Measure 40 c.c. milk into a flask of 100 c.c. capacity, add some carbonate of soda if the milk is not alkaline, and then 20 c.c. moderately concentrated solution of neutral acetate of lead, and shake well; having next fitted the neck of the flask to a long glass tube or to the condenser of a Liebig's still, boil it over a small flame; then filter and test the filtrate with the polariscope (p. 85). With a 1-decimetre tube the percentage of sugar is obtained by multiplying the rotation by 1·44.

BOOK IV.

EXCRETA: THE FÆCES AND URINE.

CHAPTER I.

THE FÆCES.

In the fæces are contained the undigested parts of the food swallowed, as well as the different excreta of the bile and intestinal secretions; and accordingly its composition will vary very much according to the nature of the diet. The *color* of the fæces also varies, being due to the more or less altered biliary pigments, but depending largely on the nature of the food, having a dark brown color with an exclusive meat diet, a yellowish brown with a mixed diet, and a yellow with a milk diet. In diarrhœa the fæces are generally light in color, and in jaundice they may be quite colorless. The *smell* depends largely on the indol and skatol, and to a less degree on the valerianic and butyric acids and the sulphuretted hydrogen present. The *reaction* is neutral or alkaline, though occasionally acid, but it depends greatly on the character of the food: with an exclusively meat diet the acid reaction continues longer in the small intestine than with a vegetable diet (BERT).

Amount.—In man the fæces form $\frac{1}{7}$ to $\frac{1}{8}$ of the fresh solid food[illegible]s ingested, averaging about $5\frac{1}{2}$ oz. (LIEBIG); or the dried fæces with [illegible] a nitrogenous diet, about $\frac{1}{10}$ to $\frac{1}{14}$ of the food calculated in the dry state, but about $\frac{1}{6}$ to $\frac{1}{8}$ with a bread diet (BISCHOFF and VOIT with dogs) [illegible]). The quicker the food passes through the intestine the greater is the absolute amount of fæces.

Chemical Composition.

General Components. 1. *Parts of the Ingesta.*—(*a*) Solids 17·4 to 31·7 per cent. and water 68 to 82 per cent.

(*b*) *Salts.*—Chiefly soluble salts of the alkaline earths; but in diarrhœa, etc., also salts of the alkalies. When the reaction is alkaline or neutral triple phosphate is constantly present.

(*c*) *Portions of food* (1) *undigested*, either from being in excess, as in the case of starches, fatty bodies, and crude albumens; (2) *imperfectly digested or absorbed*, as fatty emulsions or fatty acids, leucin, tyrosin, etc., and occasionally traces of albumen (these are much increased in diarrhœa); (3) *difficult of digestion*, as crude starches, tendons, elastic tissue, earthy phosphates, triple phosphates, etc.; and (4) *non-assimilable*, as cellulose, chlorophyll, gums, resins, epitheliums, and insoluble salts.

2. *Excreta of the Biliary or Intestinal Secretions*, as mucus, part of the glycocholic acid, and the decomposition products of part of the taurocholic acid, as taurin, cholic acid, and dyslysin; together with the biliary pigments, hydrobilirubin or stercobilin, and biliverdin, cholesterin or its derivative (?) stercorin (FLINT), and epithelial cells, etc.

3. *Certain Decomposition Products*, some of doubtful origin, but more or less characteristic of the fæces, as excretin, indol, skatol, naphthylamine, and excretolic acid; also some of the higher fatty acids, as well as acetic, valerianic, isobutyric, and lactic acids, partly free, but in great part generally combined with ammonia or other bases. Dry distillation of the fæces furnishes much ammonia and a trace of trimethylamin.

I. *Analysis of the Fæces*—with a bread and animal diet (BERZELIUS).

Water	75·3
Parts soluble in water	5·7
Bile	0·9
Albumen	0·9
Extractives	2·7
Salts	1·2
Insoluble constituents	21·0
Undigested food	7·0
Mucus, fat, etc.	14·0

II. *Ditto* (WEHSARG).

Fluids	68·3 to 82·6
Solids	31·7 " 17·4
Ether extractives	11·5
Alcoholic "	15·6
Watery "	20·0

III. *Inorganic Constituents* (ENDERLIN).

Earthy phosphates	80·37
Silica	7·94
Calcic sulphate	4·53
Sodic phosphate	2·63
Ferric "	2·09
Sodic chloride and sulphate	1·37

These vary from 16 to 57 grams (4 to 14½ drams) in the 24 hours.

IV. *Ultimate Percentage Composition with a Meat and a Bread Diet.*

	Meat diet.	Fæces.	Bread diet.	Fæces.
C	51·95	43·49	45·41	47·39
H	7·18	6·47	6·45	6·59
N	14·11	6·50	2·39	2·92
O	21·37	13·58	41·63	36·08
Salts	5·39	30·01	4·12	7·02

V. The loss by the fæces in carbonic acid and nitrogen varies very considerably according to the food taken, thus (RUBNER):—

	Carbohydrates in the food.	Loss per cent. of carbonic acid in the fæces.		Nitrogen in the food.	Loss per cent. of nitrogen in the fæces.
White bread	391 to 670	1·4 to 0·8	Beef	40·0 to 48·8	2·5 to 2·7
Rice	493	0·9	Milk	12·9 " 25·8	6·5 " 12·0
Potatoes	718	7·6	White bread	7·7 " 13·0	18·7 " 25·7
			Rice	8·4	25·1
			Potatoes	11·4	32·2

VI. Fermentation changes, some of which are closely allied to decomposition processes, undoubtedly occur in the intestine, as proved by the presence of free hydrogen; we find even that chyme removed from the body, but maintained at the normal temperature, continues to evolve both carbonic acid gas and hydrogen.

As will be seen by the following table, the nature of the diet affects the composition of the gases.

(*a*) *Small Intestine* (PLANER).

	Bread diet.	Leguminous diet.	Meat diet.
	Per cent.	Per cent.	Per cent.
CO_2 . .	38·8	47·3	40·1
N_2 . . .	54·2	4·0	45·5
H_2 . . .	6·3	48·7	13·9
O_2 . . .	0·7	0·0	0·5

(*b*) *Large Intestine* (PLANER).

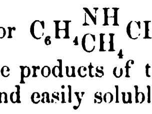
	With meat diet.	Leguminous diet.
	Per cent.	Per cent.
CO_2 . . .	74·2	65·1
H_2 . . .	1·4	2·9
H_2S . . .	0·8	
N_2 . . .	23·6	5·9

(RUGE.)

	Milk diet.	Leguminous diet.	Meat diet.
	Per cent.	Per cent.	Per cent.
CO_2 . . .	16·8	21·0	8·4
N_2 . . .	38·3	18·9	64·4
CH_4 . . .	0·9	55·9	26·4
H_2 . . .	43·3	4·0	0·7
SH_2 . . .	traces		

A small part of the carbonic acid, and possibly the chief part of the nitrogen, come from the swallowed air, the rest of the nitrogen being derived probably from the blood or from the splitting up of some of the proteids. Hydrogen is evolved in the butyric acid fermentation, and most likely also in some of the proteid decompositions occurring in the intestine. Carburetted hydrogen has never been found in the intestinal gases of dogs or cats by HOFMANN.

The *meconium*, or the contents of the intestine of the new-born child, forms a dark greenish brown, or almost black, viscid mass, generally with an acid reaction; it contains biliary acids more or less altered, bilirubin, biliverdin, cholesterin, and mucus; sulphates also are abundant, and calcic and magnesic phosphates, oxide of iron, and sodic chloride. White cells, generally green-stained, cylindrical epithelial cells, intermixed with fatty drops and cholesterin crystals, are likewise to be seen under the microscope. *On analysis* it yields about 20 to 27 per cent. solids, 1 per cent. ash, ¾ per cent. fats, and ¾ per cholesterin (ZWEIFEL).



INDOL, C_8H_7N or $C_6H_4{\genfrac{}{}{0pt}{}{NH}{CH_4}}CH$.—This body belongs to the aromatic series, and is one of the products of the putrefaction of albumen. It is soluble in boiling water and easily soluble in alcohol and ether. Formed in the small intestine, it is in part excreted in the fæces, but part is absorbed and appears in an oxidized form in the urine as indoxylsulphuric acid or indican ($C_8H_7NSO_4$).

Preparation.—Place in a large flask 300 grams albumen with 4·5 litres of water; add to this 300 grams finely divided ox pancreas, and digest the whole over a water bath at 40° to 45° for 70 hours continuously. Then strain through linen, acidify with acetic acid, and distil in a tubulated retort over a sand bath to one-fourth the volume of the liquid. The filtered distillate is next to be rendered alkaline with liquor potassæ and well shaken with its own volume of ether, and the ether decanted. On distilling the ethereal extract an oily substance remains behind, to which a little water is to be added; it is then boiled and allowed to crystallize.

Properties.—It forms large, pearly, colorless crystals, soluble in boiling water and in alcohol and ether. The dilute solution on the addition of chromic acid gives a voluminous, dark violet brown precipitate which is insoluble in ether, chloroform, and benzol, but easily soluble in hydrochloric acid, forming a violet solution. If to a solution of indol in benzol picric acid is added, needles of indol picrate are formed. Under the action of ozone a portion is converted into indigo blue.

SKATOL is a constant constituent of the fæces (BRIEGER), and appears as a putrefaction product of albumen. *It can be obtained* by extracting fresh fæces with the third of its weight of water, acidifying with acetic acid (30 grams to each kilo. of fæces), and distilling off most of the added water. This distillate is heated with sodic carbonate and well shaken with ether; the ethereal extract is evaporated and the residue boiled in some water. From the hot filtrate almost pure skatol crystallizes out in delicate plates that have a well-marked fæcal odor.

Treated with a drop of hot, fuming nitric acid, it gives no red precipitate like indol, but a whitish cloudy one; and from its hydrochloric acid solution it is thrown down by the addition of picric acid in the form of red needles.

EXCRETIN, $C_{20}H_{36}O$ (HINTERBERGER), is a cholesterin-like body that exists in fæces in very small amount.

It is prepared by exhausting fresh fæces with boiling alcohol (90 per cent.), filtering after a week, and precipitating the filtrate with milk of lime. The precipitate is dried and exhausted with a hot mixture of alcohol and ether; the extract after several days, deposits yellow crystalline needles of excretin, which can be purified by recrystallizing them from alcohol (95 per cent.)

Pathology.—Different abnormal constituents may be met with in the fæces, chiefly abnormal, however, from being in excess.

Albumen and mucus occur in the evacuations of cholera, typhoid fever, and dysentery, the mucus increasing particularly in catarrh of the intestinal tract and in hæmorrhagic affections.

Bile may be absent in jaundice, etc., causing the fæces to have a light color; or it may be present in excess, and more or less unaltered, as in some forms of diarrhœa.

Blood and pus appear in dysentery, and occasionally in typhoid fever and cholera.

Epithelium is greatly increased in the evacuations of cholera and dysentery.

Fats show themselves in disease of the pancreas, obstruction to the flow of bile, and in different cachexias, as phthisis, etc.

Leucin and tyrosin can be detected in cholera evacuations.

The *salts* are increased in intestinal fluxes of different kinds.

Urea and alloxan are abundant in intestinal catarrh, uræmia, and some of the eruptive fevers. The urea, unless rapidly discharged, is decomposed into ammonic carbonate.

Microphytes, such as vibrios, zoöglea, sarcinæ, etc., are met with in different morbid conditions.

The administration of calomel and certain ferruginous mineral waters may render the fæces of a green color; the fæces may likewise assume a black tint from the presence of altered blood or under the influence of salts of iron.

Intestinal concretions are occasionally met with, particularly in the colon of herbivora, rarely, however, of man. In horses they often attain a large size. They consist generally in great part of earthy phosphates, but sometimes chiefly of fatty matters, and occasionally of insoluble animal matters, as hairs, or of vegetable fibres. The term *bezoar* has been applied to these intestinal concretions. In some animals two of the components are peculiar, and have been described as *lithofellic* ($C_{20}H_{36}O_4$) and *bezoardic* ($C_{14}H_6O_8+2H_2O$) acids, the latter being a tannin derivative. A concretion from a horse had this composition:—

	Per cent.
Triple phosphate	90·0
Organic constituents	3·2
Silica	5·2
Earthy salts	4·2
Oxide of iron	1·0
Sodic chloride	0·5
Sulphuric acid	0·5
Soda	0·4
Lime	0·2
Phosphoric acid	0·2

Scybalæ consists of masses of mucus mixed with excrement and forming nodosities.

CHAPTER II.

THE URINE.

General Characters.—Normal urine has a pale straw yellow or amber tint, and is acid, clear, and limpid when passed, but after some time deposits traces of mucus mixed with epithelial cells (the *mucous cloud*); its temperature after emission varies between 35° and 37°, this of course depending on the temperature of the body, as in such diseases as scarlatina and the cold stage of intermittent fever it is much above the normal. When shaken a slight foam forms on the surface, but this quickly disappears unless much sugar or albumen is present, when the foam is more permanent. After some 24 hours or so there is often a deposit containing uric acid, partly in an amorphous and partly in a crystalline form, and sometimes also crystals of oxalate of lime, etc.

A. **Reaction.**—This is normally acid, though some urines show what is termed the amphoteric reaction, giving both the acid and alkaline reactions to test paper, owing probably to the presence of acid phosphate of soda; but the acidity diminishes after the urine has stood some considerable time, although a temporary increase in the acidity first occurs—the so-called *acid fermentation* of Scherer. A neutral or amphoteric and then an alkaline stage is reached after some days or even weeks have passed (*alkaline fermentation*), when the urine loses its transparency, acquires an ammoniacal odor, and a deposit occurs of triple phosphate ($MgNH_4PO_4 + 6H_2O$) and urate of ammonia [$C_5H_2(NH_4)_2N_4O_3$], together with bacteria in great numbers, its surface also being covered with an iridescent film in which lie crystals of triple phosphate. During this stage part of the urea decomposes into ammonic carbonate, some of which combines with uric acid and some taking part in the formation of triple phosphate. This fermentation change in the urine depends, no doubt, in part on the presence of bacteria together with much mucus. Accordingly, if urine has to be kept some time before being examined it is advisable to preserve it in well-stoppered clean bottles, and some advise also the addition of a little salicylic acid, thymol, or hydrochloric acid. The presence, however, of cystin or of much pus or mucus induces rapid fermentation.

The temporary increase in the acidity, according to Röhmann, occurs only in exceptional cases, depending then probably on the presence of sugar, alcohol, or other bodies yielding acids by fermentation.

The *acidity*, according to Liebig, is due to the presence of the acid phosphates of soda and potash (NaH_2PO_4 and KH_2PO_4); probably also the acidity may be due in part to the acid urates and to the free carbonic, uric, and hippuric acids present (Byasson), although little or no free acid can be detected by sodic hyposulphite.

Sometimes after a large meal the acid reaction of the urine is lessened, and it may even become distinctly alkaline. *The reaction, indeed, is closely related to the digestion of food* (Bence Jones), an alkaline tide, as Dr. Roberts terms it, setting in after meals, whether of animal or vegetable food, appearing sooner after breakfast than dinner, but not being so intense nor lasting so long as after the latter meal. In the third and fourth hour after dinner the reaction is generally alkaline, and the urine is rich in alkaline and earthy phosphates. But the ultimate effect of food, particularly animal food, is temporarily to increase the acidity. To detect the alterations in the acidity the urine should be voided at frequent intervals after the meals and tested at once. The change in the reaction is probably due to the abundant formation of hydrochloric acid in the stomach during digestion, and to the entrance of the alkaline bases of the food into the blood at the same time. In the formation of the acid, basic sodic phosphate is formed,

$$NaCl + Na_2HPO_4 = HCl + Na_3PO_4,$$

which is eliminated by the kidneys, rendering the urine neutral or alkaline.

The *maximum of acidity* is during the night. In new-born children the urine has normally a neutral, or exceptionally a weakly acid reaction. *Alkaline urine* is generally clear when emitted, but it soon becomes covered with a pellicle containing crystals of calcic phosphate, and triple phosphate crystals are abundant in the deposit.

Vogel regards the *amount of acidity* of the total urine of the 24 hours as equivalent to 2 to 4 grams of oxalic acid, Kerner as equivalent to 1·949 gram. The mean total acidity would be neutralized by 1·5 gram sodic hydrate (Rayer).

The urine of carnivora is generally clear, and strongly acid and of high specific gravity, while that of herbivora is alkaline, of low specific gravity, and often turbid from the presence of phosphates and carbonates.

The *degree of acidity*, we have seen, varies somewhat with the digestion. With a flesh diet it is very acid, during starvation only weakly so. Strong muscular exercise increases it (**Klüppel**), as also the administration of mineral acids. In febrile conditions an *increased acidity* occurs, particularly at the beginning of such severe fevers as typhus and rheumatism, the total volume of the urine, however, being diminished at the same time; also after asthmatic attacks in emphysema, and in pneumonia and pleurisy. The urine is *alkaline, or less acid*, after the use of hot baths or of prolonged cold baths (**Duriau**); after profuse acid sweating; after the copious ingestion of vegetable acids or their salts, as alkaline carbonates, tartrates, etc., in vegetable food; in decomposition of urine in the bladder from retention occurring in old-standing disease of that organ; occasionally in nervous debility, in some forms of cerebral disturbance, chlorosis, anæmia, general debility, abundant acid vomiting, and in certain anæmic conditions occurring in the beginning of convalescence after many diseases. In these last the alkalinity is due to a fixed alkali, and may be associated with a deposit of amorphous phosphate of lime. But the urine may be alkaline from the presence of ammoniacal salts, as in the more or less decomposed urines occurring in pyelitis and cystitis, or where there is a tendency to retention of the urine, as in paraplegia, foreign bodies or new growths in the bladder, stricture or obstruction of the urethra, etc. As a general rule the urine is not alkaline when secreted, but becomes alkaline in the bladder as the result of a decomposition of its urea. Such urine always deposits a sediment, generally of phosphate of lime and triple phosphate, and its odor is ammoniacal and often offensive.

It is easier to render the urine alkaline than to increase its acidity.

To Estimate the Acidity.—This can be effected approximately by titrating the urine with a *normal* solution of caustic soda, which is prepared by dissolving the equivalent weight in grams ($NaHO = 40$) of this body in a litre of water; accordingly each c.c. = 40 milligrams or 0·04 gram. In the same way a normal solution of oxalic acid ($C_2H_2O_4 + 2H_2O = 126$) will contain 63 grams in the litre—that is, half the equivalent, as the acid is dibasic.

As we cannot prepare the caustic soda solution directly by weighing, owing to the varying amount of water present in it, we have recourse to titrating a solution of it by means of a standard normal solution of such an acid as the oxalic. The latter is first prepared by dissolving 63 grams of pure, well crystallized, and thoroughly air-dried oxalic acid in 1,000 c.c. water. The 150 to 155 grams NaHO are weighed and dissolved in about 1,050 c.c. water and well shaken up. The *indicator* has next to be got ready. A solution of litmus can be employed for this purpose, but a solution of cochineal or of rosolic acid acts better. The *rosolic acid* is added to alcohol until a strong orange solution is obtained; a couple of drops of this is added to the solution to be titrated. The *cochineal solution* is prepared by digesting 3 grams powdered cochineal in 250 c.c. of a mixture of water (4) and alcohol (1). Its natural color is yellowish red, and it is rendered violet by alkalies and restored to its original color by acids.

1. *Preparation of the Normal Caustic Soda.*—10 c.c. of the normal oxalic acid solution are placed in a small beaker, a few drops of the rosolic acid poured in, and then the caustic soda slowly added from a graduated burette until the yellow passes into a red or rosy color. The experiment should be performed at least three times, and the mean taken. Suppose that to saturate the acid 9·1 c.c. of the soda solution are required, then to every 9·1 c.c. 0·9 c.c. water is to be added, so as to obtain a solution of which 1 c.c. will correspond to 1 c.c. of the acid. Therefore to 1,000 c.c. caustic soda solution $\left(\frac{1000 \times 0{\cdot}9}{9{\cdot}1} = 98{\cdot}9\right)$ 98·9 c.c. water must be added. The chief complication to which this process is subject is due to the presence of carbonic

acid in the caustic soda, as this acid when evolved affects the indicator. Accordingly, to avoid this it is recommended to add at first only as much soda as to render the solution colorless, then to boil so as to expel the carbonic acid, after which the titration is to be proceeded with in the usual way.

2. *Determination of the Acidity of Urine.*—Take 100 c.c. of the urine and add to it from a graduated burette the normal soda solution (1 c.c. = 0·063 oxalic acid), which had best be diluted with water to one-tenth its strength (1 c.c. = 0·0063 oxalic acid). From time to time, after stirring the fluid with a glass rod, narrow slips of red litmus paper are introduced, and the addition of the caustic soda continued until the litmus paper begins to turn blue. Or violet litmus paper may be streaked with a thin glass rod moistened with the mixture, and the addition continued until no change of color is produced.

If, say, 13 c.c. of the diluted soda solution were required, then the acidity of the 100 c.c. urine is $13 \times 0·0063 = 0·0819$; and for the total urine of the 24 hours—say 1,500 c.c.—the acidity expressed as oxalic acid is therefore equal to 1·2185 gram.

The presence of the acid phosphate of soda in the urine, it should be remembered, renders the result merely approximative.

B. **Color.**—Normal urine possesses a clear amber yellow color, that passed in the morning being generally darkest in tint. The color deepens as the urine stands, and depends on the nature of the food, and in part on the age and character of the individual. In very young children the tint is very slight, and the larger the quantity passed in adults the paler it becomes. It is *pale in color*, as in the *urina potus* of health, in anæmia, chlorosis, and diabetes, and in the reconvalescence after severe acute affections. It is very *rich in color* in acute fevers, just as is seen normally in the *urina chyli* of health and after profuse sweating with little ingestion of water. The presence of bile pigments imparts a brownish coloration accompanied by a greenish tint, that of blood or its pigments a reddish coloration; in chyluria it is yellowish white, and in melanotic cancer greenish yellow, turning to a dark brown or black. Sometimes the surface presents a blue color, from the presence of indigo. Certain drugs and vegetables likewise affect the color; thus the urine is blackish after phenol, dark also after gallic acid, brownish yellow after santonin, intensely yellow after chrysophanic acid, rhubarb (changed to red by ammonia), senna, logwood, madder, beet root, and bilberries. The coloration by these vegetable pigments is changed to a blood red by alkalies, and the yellow tint restored by acids.

To remove the color of urine it may be filtered through animal charcoal, or precipitated with basic lead acetate or milk of lime, or digested with zinc and hydrochloric acid.

C. **Transparency.**—Normal urine is always clear, but occasionally, and particularly in abnormal conditions, it is turbid. For the first four or five days after birth a child's urine is somewhat turbid, owing to epithelium, mucus corpuscles, urates, and occasionally oxalate of lime. Urine may be *turbid when passed*, and this indicates an excess of mucus, or the presence of renal epithelium, pus, blood, chyle, semen, bile, or phosphate or urate of soda in excess, etc. A turbidity shortly subsequent to the passage of the urine is generally the result of the precipitation of phosphates or urates, or it may result from fermentation or decomposition. But even normally a turbidity may show itself some hours after the urine has been passed.

D. **Quantity.**—In the 24 hours 1,500 to 1,700 c.c. (about 52½ to 59½ oz.), increasing with general functional activity and diminishing during sleep. It may be increased to 2,000 or even 3,000 c.c. when much fluid has been ingested, or it may sink to 800 or 900 c.c. Women also secrete, as a rule, less than men. The amount depends considerably on the blood pressure in the kidneys. This, we know, is raised by increased force and frequency of the heart's beat, and by constriction of the vessels supplying other parts of the body, as the skin, particularly if accompanied by a relaxation of the renal artery; while it is diminished by a lowering of the general blood pressure either from diminished cardiac activity or by a dilatation of other vascular areæ of the body.

Section of the spinal cord below the medulla leads to an arrest of the secretion by causing a general vascular dilatation; irritation of the spinal cord effects the same thing, but by causing a general constriction of the vessels, the renal arteries included. Section of the renal nerves likewise leads to polyuria, also section of the splanchnics, but to a less extent, possibly through division of the vasomotor nerves of the kidney; while stimulation of the splanchnics arrests the flow (after FOSTER).

Different names have been given to the urine voided at different times of the 24 hours. Thus *urina potus* is that passed after much fluid has been drunk, as in summer; it is pale in color and of low specific gravity. The ***urina cibi*** is that excreted soon after a meal; it is darker in color and of high specific gravity. The ***urina sanguinis*** is that formed during the night and voided in the morning.

The quantity is affected by the food and fluids ingested, and by the secretive energy of the skin and lungs, being always increased after meals and nervous activity, and diminished by sleep. The influence of age is considerable. At the end of the first month the daily excretion of urine is about 200 to 300 c.c., and from three to five years a mean of 750 c.c. in boys and of 700 c.c. in girls. While in the child (from three to seven years) the amount of urine in the 24 hours for each kilo. (2·2 lbs.) of body weight averages about 59 c.c., in middle age (30 to 60 years) a healthy adult drinking abundantly of fluids only secretes about 24 c.c. per kilo.; that is, the activity of the secretion is about 2·5 times greater in the early period.

Urine of Children (SCHABANOWA).

Age.	Quantity.	Sp. gr.
2 to 4 years	17·5 oz.	1011
5 " 9 "	36·5 "	1013
10 " 13 "	50·5 "	1012

In certain conditions the urine is greatly *increased* in amount, constituting *polyuria*, which is present in diabetes insipidus and mellitus, in granular contracted kidney with cardiac hypertrophy, in the early stages of waxy kidney, and it may occur after the absorption of œdematous fluids or exudations, in the convalescence of fevers (*epicritical polyuria*), and in certain disturbances and alterations of the nerve centres, as in cases of hysteria, chorea, epilepsy, etc. On the other hand it is *diminished*, or even occasionally *absent* (*anuria*, *oliguria*), in cases of weakened heart action from degeneration, or in valvular disease leading to passive congestion of the kidney; in emphysema, etc., of the lung in which the circulation is retarded; also in all acute inflammatory processes, profuse sweating, etc., and cases where there is excessive discharge of water by the intestine, as in diarrhœa, enteritis, and cholera. Further, a diminution has been noted in the following: lead poisoning; ***eclampsia parturientium*** depending on spasm of the renal arteries (COHNHEIM); mechanical compression or closure of the ureter; filling up of the renal tubes with casts, etc., as in nephritis, a diminution being present in the last stage of all forms of Bright's disease; during the collapse of cholera, and in cirrhosis of the liver.

It should be remembered that for *accurate quantitative analyses* the whole urine passed in the 24 hours must be preserved in the same vessel, and a specimen of this used; for the amount passed, say in an hour, cannot be taken as a guide, as normally in one hour only 20 c.c. may be secreted, and in another hour as much as 200 c.c. Further, in noting the total quantity of urine in the day, the amount of fluids ingested should be recorded, as well as the presence of fluxes from the skin or bowels.

E. Specific Gravity.—It is of more importance to ascertain the specific gravity of the total urine passed in the 24 hours than of a portion of it passed at any one act of micturition. As the specific gravity depends on the amount of solids present, a high specific gravity indicates a large percentage of solids. Indeed, an approximation to the solids present may be made by multiplying the last two numbers of the specific gravity by 2·33 Thus a urine having a specific gravity of 1018 would contain (18 × 2·33 = 41·94) 41·94 grams of solids in the 1,000 parts. Fairly accurate results will be obtained by substituting 2 for 2·33, as, besides being easier to use and remember, it is a mean of the different numbers that have been proposed for the purpose. But there are cases where the results thus obtained are very erroneous, and accordingly if a correct estimate is required the solids obtained by evaporating a certain volume of the urine should be weighed.

Variations.—Copious ingestion of fluid *lowers* it greatly, and much vomiting and purging may not only lessen the amount of urine but also its specific gravity. After attacks of hysteria it may be temporarily as low as 1003. A low specific gravity generally indicates a deficiency in the excretion of the waste products, as in hydræmia, anæmia, and chlorosis; albuminous urine also is generally of low specific gravity, 1010 to 1012. A child of a month old has a urine with a specific gravity often as low as 1003. At birth it is about 1010; then it sinks, so that about the tenth day it may be 1002, when it gradually begins to rise again. With the same individual also the proportion of solids may vary normally as much as one-third more or less from day to day.

The specific gravity is generally *raised* when the urinary secretion is lessened, as in fevers, but the contrary is the case in polyuria. In most chronic diseases the solids are diminished and the specific gravity lowered. In the acme of acute inflammatory processes, while the total solids may be only 40 grams in the 24 hours, yet, on account of the lessened excretion of water, the specific gravity is higher than normal. It is also raised in the scanty urine of acute renal dropsy. An increased specific gravity with an increased excretion of urine should be regarded with suspicion, being generally associated with diabetes, in which disease it is often as high as 1040 to 1050. With excess of urea it may rise to 1030 or even higher. *Little urine with increased specific gravity* indicates diminished secretion, other watery effusions, or the presence of some morbid process; *much urine with a low specific gravity*, abundant ingestion of water or absorption of exudations or effusions, also some forms of diseased kidney; *little urine with a low specific gravity*, uræmia and some forms of Bright's disease, particularly in the later stages; and *quantity much increased with a high specific gravity*, diabetes.

To Take the Specific Gravity.—This is usually done by means of the urinometer. The urine is poured into a long, narrow, cylindrical glass and the urinometer inserted. The latter should be made to sink slowly into the urine, and when it has come to rest read off at the level of the fluid. The cylinder must be sufficiently wide to permit of the urinometer floating freely without touching; and before the urinometer is inserted it should be carefully dried if necessary, and if any particles of air adhere to it while in the urine, these are to be wiped away with a feather; any froth also on the surface of the urine is to be previously removed with a slip of filter paper. The temperature of the urine should be about 15°, as the urinometer is generally constructed to give accurate indications at this temperature; if below this point the specific gravity obtained is too high by about 0·1° for each degree down to 7°; and too low, above 15°, by an average of 0·1° for each degree up to 18°, and from that to 25° by an average of 0·2° for each degree.

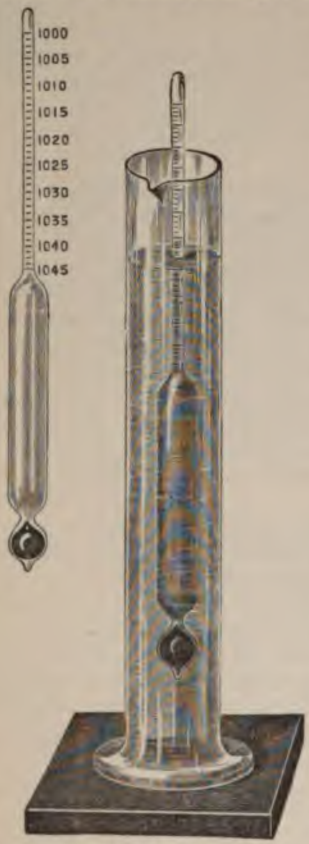


FIG. 28.—URINOMETER.

If the urine is in too small quantity to admit the use of the urinometer, specific gravity beads or bottles may be employed.

To obtain accurately the amount of solids is a difficult operation, owing to the hygroscopic character of the residue and to the decomposition of the urea present in it when sufficiently heated to expel all the moisture. One of the following plans may be adopted: (1) Evaporate 5 c.c. in a small weighed platinum capsule over a water bath, and weigh the residue after it has been dried for some time in an air bath at 115° and then cooled over sulphuric acid. Only a roughly approximative estimate is thus obtained. (2) Remove 5 c.c. of the urine with a pipette, and evaporate it in the receiver of an air pump in a weighed capsule placed over a dish containing strong sulphuric acid. Leave for 24 hours *in vacuo*, then weigh; and the weighing may be repeated after another 24 hours over fresh sulphuric acid in the exhausted receiver.

(3) *To obtain the ash*, 50 c.c. urine are evaporated to dryness in a weighed platinum crucible over a water bath, and then carefully heated in the flame of a Bunsen burner. Add a little water to the capsule when cool, then warm it and throw the contents upon a small filter that has been previously treated with hydrochloric acid and well washed; repeat the washing of the capsule, filter, and collect the filtrate and washings. The filter and its contents are next to be heated to dryness, and the dry filter exposed to a red heat in a platinum capsule. The ash will soon be reduced to whiteness, as the alkali salts, which hinder the burning of the carbon, have been removed by the washing. The filtrate and the washings are now to be added to the same capsule and to be evaporated to dryness; the dry residue is finally heated to redness, allowed to cool in an exhausted receiver over sulphuric acid, and weighed.

The ratio of the mineral to the organic residue varies somewhat, but in healthy urine it is generally in the proportion of 1 to 1·2 or 1·7; while in abnormal urine the ratio may be 1 to 2, 2·5, or 4; that is, there is a higher proportion of organic matter (WANKLYN).

F. **Odor.**—Fresh urine has a faintly aromatic smell, which soon, however, disappears; it becomes ammoniacal when the urine decomposes. Its characteristic odor may be altered by the ingestion of certain foods, as hare, asparagus, garlic, turpentine, saffron, balsam copaiba, cubebs, assafœtida, valerian, etc.

CHAPTER III.

CONSTITUENTS OF URINE.

THE secretion of urine is a double process, partly filtration and partly excretion, this last being less dependent than the former upon alterations in the blood pressure. By *filtration*, which occurs chiefly in the Malpighian capsules of the kidney, the bulk of the water and of certain soluble bodies are eliminated; and by *excretion* the great proportion of the solids with only a small part of the water in the tubules by means of their epithelial investment, this last process being greatly dependent on the stimulating presence of certain bodies in the blood, such as urea, etc.

The urine is the chief means by which the decomposition products of the albumens are excreted. The members of the aromatic series in it can all be traced back to this source. The sulphur of the albumen is probably in part oxidized, and gives origin to some of the combined sulphuric acid of the urine. Traces also of the decomposition products of the lecithin, nuclein, and glycerin phosphoric acid of the nerve substance show themselves: probably part of the phosphoric acid of the urine is thus derived. In addition there are traces of the decomposition products of the carbohydrates and of sugar itself. Elsewhere reference will be made in more detail to the origin of the different urinary constituents, and it will be seen that the true function of the kidneys is chiefly excretory—that is, they are mainly occupied in discharging from the blood certain waste products that have been carried to them from other tissues or organs. These bodies may be classified into—

A. *Organic.*—1. *Bodies belonging to the fatty series*—urea, uric acid, xanthin, hypoxanthin, kreatin and kreatinin; oxalic, oxaluric, glycerophosphoric, and lactic acids.

2. *Bodies belonging to the aromatic series*—hippuric, benzoic, phenolsulphuric, indoxylsulphuric, and skatolsulphuric acids.

3. Such bodies as urobilin, extractives, and organic bodies containing sulphur, etc.

B. *Inorganic.*—Sodium chloride, alkaline sulphates and phosphates, phosphates of lime and magnesia, silicic acid, ammonia, iron, nitric acid, and such gases as carbonic anhydride, nitrogen, and oxygen.

Of these the important constituents are urea and sodium chloride, which normally bear to each other the proportion of 2 to 1, but in febrile conditions may be altered to 30 to 1.

Normal Urine of the 24 *Hours* (after LIEBERMANN).

Constituents.	Amount in grains.	Alterations under pathological conditions.
Water	52 oz.	*Increased* in diabetes, after absorptions of effusions, and in contracted kidney, etc. *Diminished* in acute fevers, cholera, dropsies, etc.
Specific gravity	1020	*Raised* in diabetes mellitus, and occasionally in diabetes insipidus. *Lowered* in polyuria and certain cachectic conditions depending on want of food, etc.
Urea	400 to 600	*Increased* in fevers to the crisis, in intermittent fever before the cold stage, in diabetes, and after absorption of dropsical effusions. *Diminished* in dropsies, in chronic liver diseases, in Bright's disease, after fevers, and in all conditions in which tissue change is hindered.
Uric acid . . .	5 " 12	*Increased* in acute fevers, in diseases of the lungs interfering with respiration (as tubercular deposit, etc.), acute rheumatism, leukæmia. *Diminished* in diabetes, chronic gout, Addison's disease.
Kreatinin . .	10 " 18	*Increased* in acute fevers, pneumonia, etc. *Diminished* in diabetes mellitus, debility, kidney disease, etc.
Hippuric acid .	6 " 15	*Increased* in fevers, diabetes mellitus, and chorea.
Sulphuric " .	23 " 38	Having more or less the same source as urea, it will increase or diminish therewith.
Phosphoric acid	48 to 54	*Increased* in fevers, in most acute nerve affections, and in tubercle of the lung. *Diminished* in many mental diseases, especially mania, and in chlorosis.
Oxalic "	0·3	*Increased* in catarrhal jaundice and in oxalic acid diathesis.
Carbolic "	0·015	*Increased* in certain diseases of the intestines, causing constipation (ileus, etc.); but has been observed to be increased also in certain cases of diarrhœa.
Phos'te of lime.	4 to 5	*Increased* in osteomalacia, rickets, scrofula, carcinoma, long continued suppuration. *Diminished* in fevers.
Phosphate of Magnesium .	7 " 11	
Chloride of Sodium.	150 " 200 Cl = 90 to 120 Na = 60 to 80	*Increased* in fevers at the outset, and with the reabsorption of dropsical fluids. *Diminished* during apyrexia, dropsies, cholera, typhus, inflammations generally, and especially pneumonia.
Free acid (calculated as oxalic acid).	30 to 60	*Increased* during the acme of acute febrile affections (on account probably of the diminished proportion of water present). *Diminished* in most diseases affecting the nutrition and leading to a deficiency therein.
Indican . . .	0·07 " 0·3	*Increased* with diseases attended by constipation, and occasionally also in cases of diarrhœa.
Total inorganic salts . . .	200 " 380	
Potassium .	38 " 48	
Sodium .	140 " 180	
Calcium .	4 " 5	
Magnesium	2 " 3	

The Gases in Urine.—These amount on an average to 15·79 per cent., of which carbonic acid forms 87·53 per cent., nitrogen 11·22 per cent., and oxygen 0·62 per cent. (PLANER). According to PFLÜGER the proportions are the following at 0° and 760 mm.:—

	Per cent.
Carbonic acid, by exhaustion *in vacuo* . .	17·5 to 18·8
“ “ action of phosporic acid *in vacuo*	0·19 “ 0·9
Oxygen	0·09 “ 0·10
Nitrogen	1·15 “ 1·21

The carbonic acid appears to exist chiefly in a loose state of combination, probably with sodic phosphate.

Amount of Solids.—Of these the urine therefore contains nearly 42 grams (648 grains) in each litre; but they may vary from 20 to 65 grams (300 to 1,000 grains). In the twenty-four hours the solids average 55 to 60 grams (840 to 920 grains).

	Mean quantity in 1 kilo. (2·2 ℔s.)		Mean quantity in 24 hours.	
	Grams.	Grains.	Grams.	Grains.
Water	956·0	14,753	1,243	19,182
Organic constituents	27·18	419·4	35·24	544
Mineral “	16·0	247	20·2	312

In general the solids increase with the quantity of urine excreted. In all grave diseases the solids diminish in the twenty-four hours, but as the urine is also generally passed in less quantity the proportion remains nearly the same. In acute maladies the volume of urine decreases, but the specific gravity increases; and as the patient improves its volume rises, and may even pass the normal considerably. In diabetes not only is the volume of the urine but also the solids greatly increased, while in certain states of the system, as hydræmia, chlorosis, anæmia, hysteria, etc., we may often meet with simple polyuria.

CHAPTER IV.

REACTIONS AND CHARACTERISTICS OF NORMAL URINE.

1. *Acid Reaction.*—Dip into the urine a piece of blue litmus paper: it becomes red.

2. *Density.*—Pour some into a cylindrical glass and insert a urinometer: the specific gravity should be about 1020; if higher than 1025, sugar or excess of urea may be present.

3. *Uric acid and Pigment.*—(*a*) Add a little hydrochloric or nitric acid: no precipitate occurs, but the urine evolves a characteristic odor and becomes dark colored. (*b*) When the urine is carefully poured over some nitric acid in a test glass, at the point of contact of the two fluids a reddish layer forms (HELLER'S urophæin ring), and a

little above this last often a whitish layer of urates, sharply defined below but less so above. (*c*) If we add to hydrochloric acid one-third its volume of urine the mixture assumes a pale red, brownish red, or a violet to a deep coloration (indican, etc.) (*d*) Pour some strong sulphuric acid into a beaker, then about twice its volume of urine, and mix rapidly with a glass rod: a more or less dark brown color is developed. In certain chronic liver affections the color may be quite black. (*e*) Saturated solution of picric acid causes no alteration of color, but the urine remains clear for three or four hours, when a slight yellow-colored sediment appears.

4. Boil a little in a test tube: the urine remains clear, its acid reaction unaltered; but if it is neutral or alkaline a precipitate of earthy phosphates will occur, which disappears on the addition of a few drops of nitric acid.

If the urine is not transparent, but becomes so on boiling, excess of urates is present.

5. *Phosphates of the Alkalies and of the Alkaline Earths.*—(*a*) Add a few drops nitric acid to the urine and boil, then add a little barium chloride solution and boil again for some time: baric sulphate is precipitated. Now filter rapidly and treat the filtrate with excess of ammonia, when *baric phosphate* is thrown down.

(j) Confirm the presence of the alkaline phosphate by boiling some nitric acid solution of *ammonium molybdate* in a test tube, and then adding to it a little urine, when a canary yellow precipitate of ammonium phosphomolybdate is thrown down.

(ij) To a fresh portion of urine add sodic acetate and then acetic acid and a drop of ferric chloride: a yellowish white gelatinous precipitate is thrown down of ferric phosphate.

(*b*) Add ammonium chloride and ammonia in excess: a white precipitate of the *earthy phosphates* (lime and magnesia) and of *oxalate of lime*. Filter and add to the filtrate a little solution of magnesia sulphate, and a precipitate of the alkaline phosphates occurs as *triple phosphates*. (Or the next method may be adopted.)

(*c*) Add to the urine acetate of ammonia (prepared by adding acetic acid to liquor ammoniæ till the acid is in excess), and to complete the precipitation add oxalate of ammonia: a little oxalate of lime is thrown down. Now boil, filter, and to the filtrate add excess of ammonia, shaking or stirring briskly: a crystalline precipitate of the *triple phosphate*.

The tests under this head having first been applied to the urine itself should next be gone through *with a solution of the dry residue*. To effect this evaporate about 20 grams of urine to dryness, and incinerate the residue. Then boil this last with a little water and filter: the filtrate will contain the phosphates of the alkalies, and the insoluble residue the earthy phosphates.

(j) To the filtrate apply test *a*; then try test *b*, when it will be found that no precipitate is obtained. Next add to a little of the filtrate ammonium chloride, ammonia, and magnesic sulphate, when a precipitate of the *triple phosphate* will be obtained.

(ij) The part of the calcined residue insoluble in water is then to be dissolved in a few drops of nitric acid, a little water added, and the solution filtered (the insoluble residue generally consists of silica). To part of the clear solution add excess of ammonia; *phosphate of lime* and *ammoniaco-magnesian phosphate* are precipitated.

To the rest of the solution add ammonia and then excess of acetic acid and oxalate of ammonia: *oxalate of lime* is thrown down. Shake well, boil, and filter; concentrate the filtrate by evaporation, and when it is cold add ammonium chloride and sodic phosphate, stirring well: a crystalline deposit of the *triple phosphate.*

6. *Soluble Sulphates.*—Add baric chloride or baric hydrate or nitrate: a white precipitate of baric sulphate, phosphate and urate, which disappears in part on the addition of hydrochloric acid, the *sulphate* only being insoluble and remaining as a finely pulverulent mass.

7. *Urea.*—(*a*) The phosphates must first be separated before applying the following test; accordingly add to the urine barium chloride in excess, and filter off the precipitate; now add to the clear filtrate some dilute solution of mercuric nitrate, and a white flocculent precipitate consisting of a combination of urea and mercuric nitrate is obtained.

(*b*) Evaporate some urine over a water bath to a syrupy consistence; place a little of this syrup in a watch glass with an equal volume of pure nitric acid, and float the watch glass on cold water: a crystalline mass of nitrate of urea will soon form.

Digest the rest of the syrup with spirit, and then evaporate the extract obtained; dissolve up the residue in a little water, and place a few drops on two microscopic slides; insert a fine thread in the fluid on each slide, and then apply cover glasses, leaving part of the thread uncovered. To the outer part of one thread apply a drop of nitric acid, and a drop of strong oxalic acid solution to the other thread, and note the formation of crystals under the microscope.

8. *Precipitates with Lead.*—Add some solution of acetate of lead; a thick precipitate falls, consisting of chloride, phosphate, urate, and sulphate of lead, as also most of the pigment present. Filter and note the clearness of the filtrate.

9. *Chlorides.*—Add silver nitrate: a white precipitate of chloride and phosphate of silver; add a few drops of nitric acid, and the phosphate dissolves; filter and note that the silver chloride forms a white, cheesy mass that is soluble in ammonia and becomes darker on exposure to the light.

10. *Salts of Lime, Magnesia, and Ammonia.*—(*a*) Add a little sodic acetate in excess and then oxalate of ammonia: a slight white precipitate of *oxalate of lime*, which becomes more evident on boiling and is insoluble in acetic acid. Now filter and add ammonia to the filtrate, when the magnesia will be thrown down as ammonio-magnesian phosphate. (*b*) To 50 c.c. of urine add some milk of lime, then boil in a small flask and test the vapors given off with a glass rod that has been dipped in hydrochloric acid, when white fumes will be formed if ammonia is present; note the smell also, and test the reaction of the vapor with a piece of red litmus paper: ammonia will be indicated by its pungent odor and by the blue coloration of the litmus.

11. *Hippuric Acid.*—It is advisable to use cow's urine for this experiment. Boil it for some time to remove excess of pigment, and filter;

evaporate rapidly to a syrup, allow it to cool, and then acidulate with hydrochloric acid; lay aside, and after 24 hours decant from the deposited crystals. These are generally much colored from admixture with pigment. Place some of the dry crystals in a small reduction tube and heat, when a sublimation will occur of benzoic acid, an odor of fresh hay or nitrobenzol being evolved and oily red drops formed. Also examine the crystals under the microscope; they generally form fine needles.

12. *Kreatinin.*—To 100 c.c. urine add some milk of lime, and then some solution of chloride of lime to complete precipitation; filter after some time and evaporate the filtrate to a syrup; add to this about 30 c.c absolute alcohol, and after mixing well lay aside for 5 hours or so in a small beaker; then add 10 to 15 drops of alcoholic solution of chloride of zinc, and lay aside again: a precipitate of kreatinin chloride of zinc occurs by degrees. Examine the deposit under the microscope, and note the prismatic crystals or fine needles arranged in rosettes or bundles.

13. Normal urine decolorizes a weak *ammoniacal cupric oxide* solution. *Tannin* gives no precipitate with it. The addition to urine of three times its volume of alcohol (90 per cent.) causes a precipitate due chiefly to earthy phosphates. If this precipitate is dissolved in water a solution is obtained which can change starch into sugar (BÉCHAMP'S *nephrozymase*).

CHAPTER V.

UREA.

THE formula for this body is $CON_2H_4 = CO\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$; its molecular weight is 60, and it contains 46·6 per cent. nitrogen.

It is found in small proportion in the different animal fluids, tissues, and organs, being absent, however, from muscle, but especially rich in the liver (0·20 to 0·46 per cent.), although this last is denied by HOPPE SEYLER. In human blood there is present 0·142 to 0·177 per cent., though it may be as low as 0·02 per cent.; but in Bright's disease it has been found as high as 1·5 per cent. In the blood of the dog the proportion is 0·0192 per cent. (WURTZ), or 0·014 to 0·085 per cent. (PEKELHARING). Urea is the principal element of the urine, this fluid containing 2 to 4 per cent., or an average mean of 2·5 to 3·2 per cent.

Preparation. 1. *From Urine.*—(*a*) Evaporate the filtered urine to a syrupy consistence, then allow it to cool, and it is advisable to surround the vessel containing it with a freezing mixture; next add colorless nitric acid in excess, or in about the same volume as the concentrated urine, and lay aside for 24 hours. Decant and collect the precipitate on a linen filter; spread it out from this upon a porous earthenware plate, and after some time dissolve it in hot water. If it is much colored shake the solution for some minutes with animal charcoal and filter. To the filtrate add baric carbonate to neutralization, then a little caustic baryta, and pass a current of carbonic acid gas through the fluid for a few minutes [$2(CON_2H_4.HNO_3)+BaCO_3=2CON_2H_4+Ba2NO_3+H_2O+CO_2$]. Filter again, evaporate the filtrate, and having dried the impure urea thus obtained by spreading it out between sheets of filter paper, boil it in absolute alcohol, filter, and from the filtrate allow the urea to crystallize out.

(*b*) The urine, particularly that of the dog, may be thus treated: Add 1 vol. baryta mixture [saturated solution of baric hydrate (2) and of baric nitrate (1)] to 2 vols. of the urine, shake together, and filter; evaporate the filtrate to dryness, and treat the residue with boiling alcohol; filter the alcoholic solution, and from the filtrate the urea is allowed to separate. If not transparent, it is dissolved up again and filtered through animal charcoal, and the clear solution finally evaporated.

2. *Artificial Preparation.*—Powder some potassic ferrocyanide, dry it over a water bath, and rub 100 grams of it well together with 50 grams black manganic oxide; then heat the mixture to redness on an iron plate. Before it has quite cooled break the mass up in a mortar and shake it well with a warm solution of 50 grams sulphate of ammonia, heat for a few minutes, filter, and evaporate the filtrate to dryness. The urea present is separated from the alkaline sulphates mixed with it by warming the residue with a small quantity of absolute alcohol (90 per cent.) The alcoholic extract is distilled, and the urea left behind is recrystallized from boiling absolute alcohol.

General Characters.—Urea in the pure state forms long flattened four-sided prisms that are striated, translucent, and silky, and terminated by oblique surfaces. Rapidly formed crystals are generally in the form of long, fine, white, glittering needles. These crystals dissolve readily in cold water and alcohol, being about twice as soluble in these fluids when boiling, but are almost insoluble in pure ether. Urea melts at 130° and decomposes at a higher temperature.

Chemical Relations.—Urea is isomeric with ammonium cyanate (NH_4CNO), this body undergoing spontaneous conversion into it, and it may therefore be readily prepared therefrom. In the transformation energy is evolved, so that the cyanate with its molecular energy may be regarded as a type of vitally active nitrogen, and the urea as that of dead nitrogen (PFLÜGER).

Urea is generally considered to be an amide of carbonic anhydride; $OC\left\{\begin{matrix}OH\\OH\end{matrix}\right.$ carbonic acid; $OC\left\{\begin{matrix}NH_2\\OH\end{matrix}\right.$ carbamic acid; $OC\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$ carbamide.

Combinations.—Behaving in some respects like an organic base, urea combines with acids, bases, and salts. The *nitrate*, CON_2H_4,HNO_3, is formed if nitric acid is added to a moderately concentrated solution of urea, generally appearing as very thin rhomboidal or hexagonal tables, although from some urines (as occasionally in Bright's disease, etc.) it may show itself in tufts of fine needles. The crystals are soluble in water, less soluble in alcohol, and insoluble in ether and nitric acid. The *oxalate*, $(CON_2H_4)_2C_2H_2O_4 + H_2O$, is also readily formed by the addition of a strong solution of the acid to a moderately concentrated solution of urea. The crystals form rhomboidal

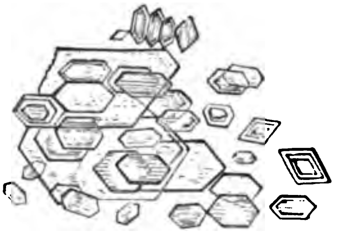


FIG. 29.—NITRATE OF UREA CRYSTALS.

Crystals of nitrate of urea—rhombic tables and six-sided plates (formed in slow crystallization).

tables or long thin prisms, and are very variable in shape. They are slightly soluble in water, and less so in alcohol. *Nitrate of mercury* combines with urea, and according to the concentration of the solutions three combinations may be formed (LIEBIG)—

$$(1)\ (CON_2H_4)_2.Hg_2(NO_3)_4;$$
$$(2)\ (CON_2H_4)_2.Hg_3(NO_3)_6;$$
$$(3)\ (CON_2H_4)_2.Hg(NO_3)_2+3HgO.$$

The last is produced when a dilute solution of the nitrate is added to a dilute (about 2 per cent.) urea solution. *Mercuric chloride* gives a white gelatinous precipitate with an *alkaline* solution of urea. *Sodium chloride* also combines with urea, $CON_2H_4,NaCl+2H_2O$, forming brilliant rhombic prisms when a solution of the two bodies is evaporated. From such a solution the urea is not completely precipitated by nitric acid.

Compound ureas are formed when the hydrogen atoms of urea are replaced by alcoholic or acid radicles; as, $CNOH$ (cyanic acid) $+ NH_2(C_2H_5)$ (ethylamin) $= CO.NH_2.NH(C_2H_5)$ (ethyl urea); $CNOH$ (cyanic acid) $+ NH(C_2H_5)_2$ (diethylamin) $= CO.NH_2N(C_2H_5)_2$ (diethyl urea); $CON_2H_4 + C_2H_3O.Cl$ (acetyl chloride) $= CONH_2.NHC_2H_3O$ (acetyl urea) $+ HCl$.

Decompositions.—Urea decomposes readily under the influence of strong alkalies and acids, organic ferments, bacteria, etc., and even by the simple heating of watery solutions—slowly at boiling point, but rapidly if heated in a closed tube to 230°, or under pressure at 100° if mixed with baryta water—the elements of water being taken up and ammonium carbonate formed:—

$$CO\left\{\begin{array}{l}NH_2\\NH_2\end{array}\right.+2H_2O=CO\left\{\begin{array}{l}ONH_4\\ONH_4\end{array}\right..$$

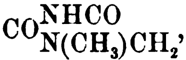
Nitrous acid, chlorine gas, and hypochlorite and hypobromite of soda decompose urea with the formation of carbonic acid, water, and nitrogen:—

$$CO\left\{\begin{array}{l}NH_2\\NH_2\end{array}\right.+N_2O_3=CO_2+2H_2O+2N_2$$
$$CO\left\{\begin{array}{l}NH_2\\NH_2\end{array}\right.+H_2O+3Cl_2=CO_2+N_2+6HCl$$
$$CO\left\{\begin{array}{l}NH_2\\NH_2\end{array}\right.+3NaBrO=CO_2+N_2+2H_2O+3NaBr.$$

The nitrous acid reaction can easily be shown by adding a few drops of nitric acid to a globule of mercury in a test tube, when pungent red fumes of nitrous acid are evolved; but if now a little urea is added only a colorless gas will be given off. If dry chlorine gas is passed over melted urea the latter is decomposed into cyanuric acid and nitrogen, hydrochloric acid and ammonium chloride also being formed:—

$$3CO\left\{\begin{array}{l}NH_2\\NH_2\end{array}\right.+3Cl_2=C_3N_3H_3O_3\ \text{(cyanuric acid)}+N_2+5HCl+NH_4Cl.$$

When heated with a mixture of caustic potash and potassic permanganate it is decomposed into carbonic acid and ammonia. If the ammonia is distilled off it can be determined in the distillate by NESSLER'S process, and the amount of urea thus estimated. Potassic permanganate oxidizes urea in acid, but not in alkaline solutions, while the inverse holds good with ozone.

Derivatives.—When melted with sarcosin urea builds up methyl hydantoin,  $CO\genfrac{}{}{0pt}{}{NHCO}{N(CH_3)CH_2}$, which is closely related to kreatin; and when melted with leucin, uramido-caproic acid is formed. Other derivatives are biuret, $(C_2O_2N_3H_5+H_2O)$, which is obtained by heating dry urea up to 150° and extracting the cooled mass with cold water; cyanamid (CH_2N_2) and guanidin (CN_3H_5).

Urea Reactions and Tests.—Make a strong watery solution of urea, and perform most of the following tests with drops placed on microscope slides:

1. Allow a drop to evaporate; when nearly dry place a cover glass upon it, and examine under the microscope: note the white silky needles formed by the crystals, generally in the form of four-sided prisms terminated by oblique facets, or as delicate six-sided superimposed plates.

2. Place a short length of thread in a drop of the solution, then cover so as to leave part of the thread outside the cover glass; now moisten the outer part of the thread with a drop of *nitric acid*, and under the microscope note the formation of crystals on each side of the thread, hexagonal tables or six-sided prisms being ultimately formed, the character of the crystals, however, being affected by their more or less rapid formation, etc.

3. Note in the same way the formation of crystals of oxalate of urea, replacing the nitric acid by a strong solution of *oxalic acid.*

4. Note the white precipitate with solution of *mercuric nitrate*, and the absence of any precipitate when *mercuric chloride* is added to an *acid* solution.

5. Place a few drops of a solution of sodic carbonate or bicarbonate in a test tube, then add a little mercuric nitrate, and a yellow precipitate is formed of mercuric hydrate.

Now to another test tube add a little solution of urea and some carbonate of soda; then pour in a few drops of the mercuric nitrate, and the white curdy precipitate is produced, owing to the urea, but no yellow color at first; after adding a little more of the nitrate, however, a yellow color appears. *So long, therefore, as there is urea present to combine with the mercuric nitrate no yellow color appears*, this occurring only with excess of the mercuric salt.

6. Cover a large crystal of urea with a drop of a saturated watery solution of *furfurol* $(C_4H_3O.COH)$ and immediately add a drop of hydrochloric acid (sp. gr. 1·1): a rapid play of colors occurs from yellow, through green to purple violet, sometimes passing into brownish black.

7. Pour a few drops into a small test tube and add a little *hypobromite of soda:* the urea at once decomposes, bubbles of gas being given off. Use hypochlorite instead of hypobromite, and it will be seen that the decomposition does not occur readily till the mixture is heated. The process is seen best by using a small test tube which is nearly filled with the hypochlorite solution, then a little urea added, and the test tube rapidly inverted over water or mercury: the nitrogen evolved collects in the tube, the carbonic anhydride being absorbed.

e *nitrous acid* for the hypobromite, and proceed as in ent: the urea is decomposed as before and gas evolved. *rate the urea from urine for examination*, evaporate a water bath to a syrupy consistence, and digest this lume of alcohol. The alcoholic extract is then evaporwatery solution of the residue tests 2 and 3 are apthe rine is albuminous it is better first to separate the ing and filtering after the addition of a few drops of acid. an excess of urea is present, in which case the specific is gene ally high, mix equal volumes of the urine and of pure d in a watch glass, which is to be floated in cold water, and of urea soon appears.

an excess of urea is not present an equal volume of pure nitric nay be added to the condensed urine, when the latter will soon me semisolid from the formation of nitrate of urea.

10. *Detection of Urea in the Blood, etc.*—The fresh-drawn blood r the serum of coagulated blood is mixed with four times its volume alcohol, by which the albumens are precipitated. Filter, evaporate filtrate to dryness, and exhaust the residue with absolute alcohol; rate this in turn, and dissolve the residue in water. Add to the ry solution some baric hydrate to precipitate any phosphates present, filter, and pass a current of carbonic anhydride through the filtrate to separate any baryta, filter, and evaporate to a syrupy consistence. Divide this syrup into three parts; add a drop of nitric acid to the first, of strong oxalic acid solution to the second, and test the third with mercuric nitrate. Then examine the first and second with the naked eye and under the microscope, and note any appearance of crystallization. If the crystals are supposed to be compounds of urea, it is well to compare them with some freshly formed crystals of the nitrate and oxalate, so as to avoid the mistake of confounding them with the crystals that frequently form of alkaline nitrates, especially in presence of extractives. Incinerate also: there is a residue with the alkaline salts, none with those of urea.

CHAPTER VI.

SOURCES AND AMOUNT, AND INFLUENCES AFFECTING THE LATTER.

Source and Seat of Urea Formation.—The urea is most probably derived from the decomposition of albuminous bodies; the amount of it excreted in the urine may therefore be taken as indicating the amount of albumen decomposition occurring in the body. According to PARKES 97 per cent. of the nitrogen of the food is thus eliminated by the kidneys. BÉCHAMP, many years ago, described the formation of urea from albumen through direct oxidation by the action of potassic permanganate in alkaline solutions, and although his statements have not been fully confirmed, he still maintains the accuracy of his former view; and in this he has been supported by **Ritter**, who obtained in the same way 0·3 per cent. from white of egg, 0·33 per cent. from fibrin, and 0·7 per cent. from gluten.

It has long been established (**Prévost** and **Dumas**) that after extirpation of the kidneys urea does not cease to be formed, but accumulates in the blood and tissues; and modern opinion is in favor of the view that instead of being formed in the kidneys it takes its origin in the blood and in the different organs of the body, particularly the liver and spleen. But it is possible that the kidneys, besides merely excreting the already formed urea, may also assist in transforming some of its direct antecedents into urea.

There is evidence of a continual formation of kreatin in different parts of the body, as in nervous tissues, muscles, spleen, etc., and it is probable that this kreatin is an antecedent of urea. Urea, although present in the blood, is not generally to be found in the parts just referred to as seats of kreatin formation.

The urea is always increased by a diet rich in proteids. In this case it is probable that an abundant formation of leucin and tyrosin takes place in the intestine, owing to a breaking down of peptones, and by their absorption and further decomposition in the liver (of the leucin at any rate) urea may be formed. In the liver much urea has been found (**Meissner**), and probably many of the metabolic processes resulting in the formation of urea here find a centre of activity. **Schultzen** is of opinion that in the normal metabolism of the proteids carbamic acid ($CO.NH_2.OH$) and ammonia are the ultimate products, and that these by their subsequent dehydration form urea, $CO_2N_2H_6$ or $CON_2H_4.H_2O$ (ammonium carbamate) — $H_2O = CON_2H_4$. It is thought probable, however, by others that all the nitrogen of urea comes to it in the form of ammonia, and that this is directly united to carbonic acid instead of carbamic acid, and subsequently dehydrated (**Salkowski**).

When an animal is fasting the tissue waste supplies the urea. Thus 100 grams of muscle substance contain about 3·4 grams of nitrogen, corresponding to 7·286 grams of urea; every gram of urea accordingly represents 13·72 grams of muscle substance, and in a fasting animal, when a day or two have elapsed, every gram of urea in the urine is equivalent to 13·72 grams of muscle waste. After fasting about 4 days a dog weighing 20 kilos. excretes about 9 to 12 grams urea. 12 grams × 13·72 = 164·6 muscle—that is, about 165 grams of daily muscle waste. If now we give to the dog about 165 grams of flesh daily, as a result the loss of weight will cease, but the excretion of urea is increased: 12 + 9 = 21 grams is about the amount of urea discharged, showing the urea due to tissue waste to be equal only to ¾ of the amount previously derived from that source. If the food is doubled, and say 165 grams × 2 = 330 grams of flesh given, the excretion is 12 × 2 + 6 = 30 grams, indicating a decrease in the tissue waste. But this holds good only up to a certain point. In cases of fevers, inflammation, etc., where the food ingested is comparatively small in quantity, and frequently not equivalent to more than 5 grams urea, a great part of the excreted urea must be due to tissue waste. Thus, take a case of pneumonia with a daily excretion of 28 grams urea; 28 — 5 = 23 grams would then arise from waste of tissue, and calculating this as muscle waste would give 13·72 × 23 = 315·56 grams of daily muscle waste.

Amount of Urea Excreted.—Among different individuals the difference in the amount excreted in the twenty-four hours is so great that it is almost impossible to strike a mean. The following estimates have been given for the twenty-four hours:—

17·5 to 23·5 grams, or	270 to 360 grains	(FLÜGGE).
30·0 " 35·0 "	460 " 540 "	(VOIT).
25·0 " 40·0 "	390 " 620 "	(VOGEL).
34·8 "	537 "	(OPPENHEIM and MEYER).

The influences affecting the amount are various.

1. *Constitution, Sex, Age, and Body Weight.*—According to most authorities the mean for healthy *men* may be taken as 34 grams (525 grains) in the 24 hours, or 0·5 gram for each kilo. of body weight; and for *women*, a mean of 25 grams (386 grains), or 0·4 gram per kilo. Calculated after UHLE'S data the urea is excreted at the rate of about 3½ grains to each pound of body weight.

In *children* the excretion of urea in proportion to the body weight is nearly double that of the adult period; but up to one month it is said only to be 0·23 gram for each kilo. of body weight (PARROT and ROBIN).

In *old age* it sinks again nearly to the half (UHLE). While, it should be observed, an increase in body weight is attended with increased excretion of urea, the two do not bear a direct proportion to each other.

2. *The character and amount of the food* has the greatest effect on the amount, this reaching its maximum some six hours after the meal, and sinking to a minimum in the early morning. The discharge of urea is in proportion to the amount of nitrogenous food ingested, and with the urea thus discharged it would appear that one-seventh of the latent or potential energy of this kind of food escapes in an unexpended state. Fasting lowers the urea by 10 to 11 grams; excessive consumption of water may raise it by 5 grams.

	Grams in the 24 hours.	
With pure animal diet	51 to 92	
" mixed "	36 " 38	
" vegetable "	24 " 28	
" non-nitrogenous diet	16	(FRANK).

In a system of experiments made by OPPENHEIM upon himself he found that on a diet consisting of 400 grams bread, 300 grams meat, and 950 grams milk the urea eliminated after four days became very constant. The mean of seven days gave 34·6 grams = 16·2 grams nitrogen; 1·1 gram was passed in the fæces. The total nitrogen in the food was = 18·9 grams, and the nitrogen excreted 17·3 grams, the difference, 1·6 gram, being retained in the body.

The maximum corresponds to the time of taking the largest amount of albuminoids as food. In the first four hours after the midday meal 0·24 gram was eliminated per hour in excess of the average; during the night the excretion fell below the average. A 24 hours' fast caused an elimination of 10 to

11 grams below the usual amount. The quantity was raised by the ingestion of large quantities of fluid and of quinine. Coffee exerted little effect, and the same was the case after excessive perspiration.

3. *The varying organic metamorphoses occurring in the body dependent on the physical and mental activity, etc.*, affect the urea considerably. But the weight of evidence is now entirely in favor of regarding *muscle work* as *not* tending to increase the amount of urea excreted (VOIT), or to do so only to a very slight extent (PARKES), and that only after *excessive* muscular exertion (NOYES, ENGELMANN); so that it is most likely that the muscle works at the expense of the carbohydrates and fats ingested instead of the albumens. It is possible that when the urea is increased during muscular exertion it may be due to some accompanying dyspnœa, and dyspnœa, according to FRAENKEL, causes an increased decomposition of albumen. KELLNER's investigations with horses, however, show that an increase in the daily work led to an increase in the nitrogenous materials excreted in the urine—an increase that disappeared when the work was lessened, and that these results ensued with food rich or or poor in proteids. But it may be stated generally that *muscle work does not produce any increase in the elimination of nitrogen unless the supply of carbohydrates for the purpose fails.* During the day there is an average excretion of 1.4 gram per hour, and during the night 1·07 gram (E. SMITH). An elevated temperature lowers the amount of urea; on the other hand an hour's immersion in a water bath at 39·5° increased the urea one-third (SCHLEICH).

4. *Influence of Drugs.*—While *diuretics* increase the amount of water they do not necessarily augment the urea. Thus *alcohol* and *digitalis* in sufficient doses diminish the urea. A similar diminution is effected by *mercurial preparations. Phosphorus* in poisonous doses lessens the urea, producing, after a time, fatty degeneration of the kidney. *Arsenic* and *alcohol* are said to produce a similar result, but the action is both slower and weaker. *Phosphorus* as well as *arsenic* probably induce a temporary increase, for after a subcutaneous injection of phosphorus in olive oil the urea is found augmented (CAZENEUVE). *Sulphate of quinine* first lessens the uric acid and then the urea; but the ingestion of 2 grams in 24 hours raised the elimination by 4 grams (MEYER and OPPENHEIM). The urea is also increase by the *mineral acids*, and by excess of the *alkaline chlorides.*

5. *Pathologically* it is both diminished and increased, a diminution indicating either a lessened activity in protein metamorphoses or a retention of urea in the body.

(*a*) The amount is *diminished* in profuse sweating, diarrhœa cholera, or any prolonged discharge from the body; in certain diseases of the kidneys, specially in the later stages of chronic Bright's disease; in most chronic, maladies or cachectic conditions, as in anæmia, leukæmia, osteomalacia, gout, and chronic rheumatism; during the period of remissions of high fevers; in severe neuralgia and certain other neuroses, as melancholia, hysteria, and catalepsy; in some diseases of the liver, especially acute yellow atrophy; and in lepra, pemphigus, etc.

(*b*) It is *increased* at the beginning of the crisis in fevers, more or less in proportion to the elevation of temperature—this is well marked in typhus. In intermittent fevers the urea and extractives increase before the setting in of the cold stage, and attain their maximum at the beginning of the hot stage. In pneumonia it increases during the febrile period, 40 to 70 grams being eliminated daily, but after about the fifth day the amount generally falls to 25 to 28 grams. In diabetes more urea is excreted than by a healthy person on the same diet, and in an amount containing more nitrogen that can be accounted for by the food ingested; an increased consumption must therefore occur in the albumen of the tissues, and the urea may rise to 150 grams (2,315 grs.)

An increase is also seen in meningitis, pleurisy, acute tuberculosis, acute rheumatism with endocarditis, pyæmia, and hepatic congestion; temporarily also during the absorption of transudations and after bleeding. In phthisis more nitrogen may be eliminated in the urea than is present in the food consumed (OPPENHEIM).

When the urine is not secreted, or if secreted is retained in any way, either from removal of the kidneys or occlusion of the ureters, etc., its constituents accumulate in the blood and organs. After a time the condition termed *uræmia* is developed, not solely, be it remembered, as the result of the retention of urea or its factors in the system, but also in part from the retention of the extractives and salts, such as the phosphates and sulphates of potash, etc. In uræmia the muscles and nerves are affected, a sense of fatigue, muscular debility, and great drowsiness being established, and finally coma terminating in death, these symptoms being generally accompanied by vomiting, cramps, and convulsions.

ZALESKY's experiments appear to show that the muscular debility and somnolence are the only constant symptoms, and that these are not dependent on the changes resulting from the decomposition of the urea into ammonium carbonate, as suggested by MUNK. Instead of an accumulation of urea or excess of carbonic acid or ammonic carbonate in the blood and tissues OPPLER and ZALESKY found a marked accumulation of kreatin or kreatinin. But other observers have noted an increase of the urea in the 24 hours of 0·026 to 0·206 and 0·276 per cent.; the results being the same whether the kidneys were removed or the ureters tied, as the distention of the tubules in the latter case soon rendered the epithelium incapable of performing its functions (GRÉHANT, GSCHEIDLEN). Part of the urea that is poured out in some of these cases into the intestine is very probably decomposed into ammonic carbonate, and possibly accounts for the cramps and vomiting. In the vomit and stools of cholera carbonate of ammonia, most likely derived in this way, is often present in abundance.

CHAPTER VII.

QUANTITATIVE DETERMINATION OF UREA.

IN any quantitative or volumetric analysis of the urine, as this fluid varies so much in composition at different times of the day and night, owing to the varying conditions of alimentation, exercise, etc., the experiments to be of value should be made with portions of the mixed total urine passed in the 24 hours. To collect the urine, vessels of two litres' capacity are generally sufficient, unless in cases of diabetes mellitus. If sediments form the supernatant liquid is employed.

A. Liebig's Method (*Titration with Mercuric Nitrate*).

In this method the mixture of urine and baryta is not neutralized during the addition of the mercuric nitrate, and the end of the reaction is determined by allowing a drop of the mixture to run into a drop of saturated soluton of sodic carbonate on a white tile, 10 c.c. of

Liebig's solution—made by dissolving 71·5 grams mercury in nitric acid and diluting up to a litre being equivalent to 0·1 gram urea.

A. *Principle of the Method.*—If to a dilute solution of urea (about 2 per cent.) a weak mercuric nitrate solution is added, an abundant white precipitate is formed, having the composition $(CON_2H_4)_2Hg(NO_3)_2 + 3HgO$, and containing urea and mercuric oxide in the proportion of 10 to 72:—

$$\begin{aligned}(CON_2H_4)_2 &= 120\\ Hg(NO_3)_2 &= 216HgO\\ 3HgO &= 648.\end{aligned}$$

Accordingly a solution of 72 grams of mercuric oxide in nitric acid and diluted to 1,000 c.c. should exactly precipitate a solution containing 10 grams of urea. $2CON_2H_4 + 4Hg(NO_3)_2 + 3H_2O = [2CON_2H_4(NO_3)_2Hg + 3HgO] + 6HNO_3$. A solution of sodic carbonate gives a yellow precipitate with mercuric oxide. If therefore a portion of the mixture of the urea and mercuric nitrate is removed and tested from time to time with the sodic carbonate, only a white precipitate will be obtained until the whole of the urea has been combined with the mercuric nitrate, and an excess of the latter is present; when this occurs a little of the mixture tested with sodic carbonate will give the yellow precipitate. To obtain this reaction, however, a slight *excess* of the mercuric nitrate must be present, according to LIEBIG 5·2 milligrams for every c.c. of the mercuric solution, or 5·2 grams for the litre. Therefore, so that each c.c. of the mercuric nitrate solution should correspond to 10 milligrams of urea and give the yellow reaction with the sodic carbonate indicator, 72 + 5·2 = 77·2 grams mercuric oxide should be present in each litre.

The following liquids and pieces of apparatus are necessary:—

(1) *A mercuric nitrate solution* of which 1 c.c. = 0·01 gram or 10 milligrams urea.

(2) *A baryta mixture* consisting of cold saturated solution of baric hydrate (2 vols.) and of baric nitrate (1 vol.)

(3) A moderately *dilute solution of sodic carbonate or bi-carbonate* to act as indicator.

(4) *A white porcelain plate*, upon which, or on a piece of glass resting on a black background, drops of the sodic carbonate solution are to be placed.

(5) *A Mohr's burette.*

(6) Three pipettes, one to contain 10 c.c for the baryta mixture; the second 15 c.c. to measure the filtrate after the precipitation of the phosphates; and the third, 20 c.c. to deliver the urine.

B. *Preparation of the Mercuric Nitrate Solution.*—The red oxide is much more difficult to dissolve than the yellow oxide, so the latter may be used in preference. The oxide is to be dried for some hours in a porcelain dish over a water bath, 77·2 grams of it weighed and dissolved with the aid of heat in as little dilute nitric acid (about equal parts of water and acid) as possible, fresh acid being added as required until the solution is completed. Excess of acid is next to be expelled by evaporating the solution to a syrupy consistence, and a little distilled water added; more and more water is gradually mixed with it, and then the whole is to be made up to 1,000 c.c. with distilled water. Often some basic nitrate separates when the dilution is made, but this is less likely to occur if the water is added very slowly at first; if it does occur the basic nitrate should be allowed to settle, and after the supernatant fluid has been decanted a few drops of nitric acid are added to the former and heat applied. The solution thus obtained is returned to the rest of the solution, which is to be made up to 500 c.c. with distilled water, then laid aside for 12 hours, and the remaining 500 c.c. water added in whole or in part, and then well shaken.

Titration of the Mercuric Solution. 1. *Preparation of* 2 *per cent. Urea Solution.*—Place some commercial urea in a porcelain dish and add to it absolute alcohol, keeping the urea in excess, so that a little of it remains undissolved; then heat over a water bath, filter the alcoholic solution and let it cool; after 24 hours pour off the supernatant liquid from the deposited crystals and dry them on filter paper. Place 2½ grams in a watch glass over some sulphuric acid under the receiver of an air pump, exhaust, and weigh after 24 hours; if any loss of weight occurs leave the urea under the exhausted receiver for another 24 hours. Now weigh 2 grams, and having dissolved it in a little water make up the solution to 100 c.c. with more water.

When pure urea can be had take 2 grams of it that has been dried at 100°, and dissolve in 100 c.c. distilled water.

2. Measure 10 c.c. of the above urea solution into a small beaker, and from a Mohr's burette let 18 c.c. mercuric solution flow into it; stir it rapidly with a small glass rod, and by means of the rod bring a drop of the mixture into contact with a drop of the dilute sodic carbonate solution spread out on the white porcelain or glass; if only a white color appears at the point of contact, then add an additional c.c. of the mercuric solution, and after mixing again remove another drop and test as before. If a yellow color *at once* appears at the line of contact of the two drops the whole of the urea has been precipitated, and we have ascertained that 19 c.c. mercuric solution = 10 c.c. urea solution.

Repeat the experiment, allowing, however, only 18·5 c.c. mercuric solution to flow into 10 c.c. urea solution, and test as before. If no yellow color appears at once on the contact of the drops, then so far the first experiment has been confirmed; and the process may be repeated to insure accuracy, adding the 19 c.c. at once.

It is necessary now to dilute the mercuric solution so that 20 c.c. (instead of 19) = 10 c.c. urea solution.

$19 : 1 = 1000 : x$. $x = 52{\cdot}6$. We therefore add 52·6 c.c. to 1,000 c.c. mercuric solution and shake well. (Of course, if the mercuric solution has been made up to 800 or 900 c.c. instead of 1,000 c.c., this must be borne in mind in making the calculation.) The solution now is of such a strength that 10 c.c. = 0·1 gram urea. It can be preserved a long time if kept in well-filled stoppered bottles.

C. *Titration of the Urea in Urine. Separation of the Phosphates.*—Add a few drops of the mercuric nitrate to a solution of phosphate of soda, and a white precipitate will be formed. Now the urine contains phosphates, which we see precipitate mercuric nitrate; therefore before attempting the estimation of urea by means of the standard mercuric solution the phosphates must first be separated. This is effected by adding to the urine half its volume of the baryta mixture.

Baryta Mixture.—This is prepared by boiling one part caustic baryta ($BaH_2O_2+8H_2O$) with 10 parts of water, then allowing the solution to cool and decanting. The solution of the nitrate of baryta is made in the same way; the two solutions thus prepared are mixed in the proportion of two parts of the caustic baryta to one part of the nitrate.

Process.—Measure 20 c.c. of the urine in a small, clean and dry beaker, and add to it 10 c.c. baryta mixture; stir well together and in a few minutes throw upon a dry filter, collecting the filtrate in another clean and dry beaker. (It is more advantageous to measure out 40 c.c. of the urine at once, and to add to it 20 c.c. of the baryta mixture. By acting in this way there will be sufficient filtrate for the two experiments required.) Take 15 c.c. of the filtrate, corresponding to 10 c.c. urine, and having placed a series of drops of the sodic carbonate solution upon the white plate allow the mercuric nitrate to flow from a Mohr's burette, in small quantities at a time, into the urine filtrate, having first noted the upper level of the fluid in the burette. After each addition stir briskly with a small glass rod, and when a distinct precipitate no longer seems to form remove a drop of the contents on the end of the rod, and bring it in contact with one of the drops of sodic carbonate. The addition of the mercuric nitrate is to be continued and the mixture tested as before until a distinct yellow color immediately appears at the point of junction of the two drops. The amount of mercuric nitrate added is then to be read off and the experiment repeated; but now the greater part of the mercuric nitrate required is to be added at once; thus: if, say, in the first experiment 18 c.c. were added before the yellow reaction was obtained, in the second experiment add 16 or 17 c.c. at once before testing with the sodic carbonate; and if in the second experiment the end reaction is obtained with 17·5 c.c., then the urine contains 17·5 grams urea in the litre, or 1·75 per cent.

Necessary Corrections. I. *More than* 2 *per cent. Urea.*—As the mercuric nitrate solution has been prepared to titrate solutions of urea containing about 2 per cent., if the urine contains much more or much less certain corrections are required before calculating the percentage. We know that to obtain the end reaction with the sodic carbonate an excess of 5·2 grams mercuric oxide must be present in the normal solution which has been titrated with the 2 per cent. urea solution. If, however, we are dealing with a urine containing, say, 4 per cent. urea, then too great an excess will be present when the terminal reaction is obtained. Accordingly we should in such a case, before testing with the sodic carbonate, add to the mixture half the number of c.c. of water that have been added of mercuric nitrate above 20 c.c. Suppose 30 c.c. were required in the first experiment, the excess is 10 c.c.; then 5 c.c. water must be added before beginning the second experiment.

II. *Less than* 2 *per cent. Urea.*—Deduct 0·1 c.c. for every 4 c.c. mercuric solution employed less than 20 c.c.

III. *Correction for Sodium Chloride.*—(j) Let the student take a dilute solution of sodic chloride (about ½ per cent.) and drop into it a few crystals of urea; now to this let him add standard mercuric nitrate. No precipitate will be formed for some time, or if a white precipitate appears it rapidly dissolves; soon, however, a permanent precipitate is formed. (ij) Let him next add a few drops of a solution of mercuric chloride ($HgCl_2$) to an acid solution of urea, and he will notice that no precipitate appears. Urea, then, is precipitated by mercuric nitrate, but not by mercuric chloride in an acid solution; and the precipitation is interfered with by the presence of sodium chloride, owing to the formation of mercuric chloride by the decomposition of the mercuric nitrate. And so long as any sodium chloride remains no precipitate of urea will occur. As the urine normally contains sodium chloride some correction must therefore be made for it. In accurate estimations the amount of this salt present should be estimated by a separate experiment but for ordinary purposes, and particularly with urines not proceeding from cases of fever or pneumonia, the correction may be applied of deducting 1·5 c.c. to 2 c.c. from the total c.c. of mercuric nitrate solution employed. In some acute diseases, on the other hand, no correction requires to be employed at all, on account of the small amount of sodium chloride present in the urine in these cases.

The chloride may also be first separated by means of the addition of silver nitrate. The solution is prepared by dissolving 29·075 grams fused silver nitrate in 1 litre distilled water (1c.c. = 0·01 NaCl). *Process:* (j) Take 20 c.c. of the urine, and having placed it in a small flask containing 40 c.c. up to a mark in its neck, add a few drops neutral potassic chromate (K_2CrO_4), and allow the silver nitrate to flow in with frequent stirring until a permanent dark red coloration shows itself, indicating the disappearance of the chloride. The mixture is then to be made up to 40 c.c. with water and thrown on a dry filter. The filtrate is to be titrated in the ordinary way, 20 c.c. being equal to 10 c.c. urine. (ij) Or, having ascertained the number of c.c. silver solution necessary to precipitate the chlorides in 20 c.c. urine, add 15 c.c. baryta mixture to 30 c.c. urine, and to 30 c.c. of the filtrate add the necessary amount of silver nitrate solution (to precipite the chlorides in the 20 c.c. of urine); this done, filter and titrate the filtrate with the mercuric nitrate. Correction must here be made for dilution.

The titration with the mercuric nitrate may also be performed at once without a previous removal of the silver chloride precipitate.

(iij) Instead of precipitating the chlorides two portions of the urine filtrate may be taken of 15 c.c. each. Neutralize one of them with nitric acid, and cautiously add the mercuric solution until a distinct cloud is produced. The other portion is to be titrated in the usual way, but before making the calculation deduct the number of c.c. required in the previous experiment to produce the cloudy precipitate.

IV. *Pathological Urine.* (*a*) *Presence of Albumen.*—If in considerable amount the albumen should be separated before employing Liebig's process. This can readily be done by boiling 100 c.c. of the urine for 10 minutes or so in a porcelain dish, after the addition of three or four drops of strong acetic acid, filtering when cool, and washing the precipitate so as to make the filtrate up to 100 c.c. It is then ready for titration when the phosphates have been removed by the baryta mixture in the ordinary way. A little urea is probably lost in the process.

(*b*) *The Urine is Ammoniacal.*—Urea, we have seen, decomposes readily into ammonium carbonate. If the decomposition has not proceeded far fairly accurate results will be obtained by direct titration; but if much ammonia is present it will be necessary to make two estimations, one of the ammonium carbonate and one of the urea still present in the urine, the ammonium salt having been previously expelled by boiling the urine for some time.

The ordinary alkalimetric process is employed in determining the ammonic carbonate, normal sulphuric acid (49 grams to 1,000 c.c. water) being employed. 50 c.c. of the urine are taken, a few drops of litmus solution added, and the acid allowed to flow in from a burette till a permanent red is obtained. To expel the liberated carbonic acid the whole should be boiled, and if the blue color reappears the addition of the acid is repeated. Each c.c. of the acid corresponds to 0·03 gram urea. 50 c.c. urine requires, say, 2·5 c.c. normal acid, therefore $100 = 5$, and as each c.c. of the acid $= 0·03$, 5 c.c. $= 0·15$ per cent. urea. This is to be added to the urea found by the direct titration with mercuric nitrate. Before doing the latter 40 c.c. of the urine are to be treated with 20 c.c. baryta mixture in the ordinary way, and the filtrate boiled for some time, the loss by evaporation being made up by the addition of water. More accurate results, however, are obtained by mixing 40 c.c. urine with 20 c.c. baryta mixture, and then distilling, the ammonia evolved being collected in some normal sulphuric acid, which is afterward titrated with normal soda solution.

(*c*) In addition to the error from the presence of sodium chloride, Liebig's process is liable to another *error from the urine containing certain bodies that precipitate the mercuric nitrate.* This may occasionally require, even in healthy urine, a correction amounting to 2, 3, or even 4 per cent. (KLETZINSKY), and in certain diseases it may rise much higher. But the error is compensated for to a certain extent by the diminished amount of sodium chloride present in many of these cases.

(j) The urine may contain *leucin and tyrosin.* If much of these bodies is present, as in acute yellow atrophy of the liver, it is better to estimate the urea by one of the methods given subsequently for the determination, as the mercuric nitrate is precipitated by leucin and tyrosin.

(ij) The accuracy of the process is interfered with by the presence of acetamid, sarcosin, glycocin, and taurin.

(iij) The process is not accurately applicable after the use of large doses of salts of potash, iodine, bromine, and chlorine, all of which act more or less in the same way as sodium chloride. Large doses of salicylic and benzoic acid are likewise detrimental.

(iv) The presence of kryptophanic acid, which precipitates mercuric nitrate, is said sometimes to interfere with Liebig's process to the extent of 5 to 10 per cent. (THUDICHUM).

As a rule, when one of these bodies is present in any quantity it is best to resort to BUNSEN'S or HÜFNER'S process, although fairly accurate results will be obtained by first precipitating the urine with neutral acetate of lead, and subsequently removing excess of lead from the filtrate by a current of sulphuretted hydrogen. The filtrate thus obtained is warmed for some time, to drive off the hydric sulphide, and then titrated in the usual way.

Modifications of the Process.—1. DRAGGENDORFF recommends the use of the chloride ($HgCl_2$) instead of the oxide. Dissolve 96·855 grams in water, precipitate with dilute caustic soda or potash, thoroughly wash the precipitate by decantation, and having carefully dissolved it in nitric acid, dilute nearly to 1,000 c.c. and titrate with urea solution (2 per cent.) in the ordinary way.

2. HOPPE SEYLER allows the mercuric nitrate to flow slowly into the urine until precipitation appears to have ceased, and then he nearly neutralizes the free acid with sodic carbonate; a drop of the mixture is next brought in contact with a drop of bicarbonate of soda solution in a watch glass placed over black paper. This neutralization is effected

from time to time, so as to maintain a tolerably constant degree of alkalinity. 10 c.c. of Liebig's solution are taken as = 0·1031 gram urea.

3. Neubauer and Voit do not neutralize with carbonate of soda, and the end reaction is determined as in the original process, but they regard 10 c.c. of Liebig's mercuric nitrate solution as equivalent to 0·1183 gram urea.

4. Pflüger considers that the fluid should be neutralized from time to time as the mercuric nitrate is added. This he effects by using a solution of sodic carbonate containing 53 grams in the litre. The carbonate is readily obtained by heating the bicarbonate for some time over a sand bath. As the indicator he uses the bicarbonate. Instead of the oxide Pflüger recommends the use of pure mercury, 71·5 grams of which can readily be measured by means of one of his tubes; or, if only impure mercury is employed, a solution of empirical strength is first prepared, and this diluted until it possesses a specific gravity of 1·0998 at 20·5°. Then by a preliminary experiment, say after Hoppe Seyler's method, the amount of mercuric nitrate is approximately obtained; in the second experiment, this amount, minus 1 to 2 c.c., is poured in, the sodic carbonate solution then added so as to neutralize the free acid, and the titration completed. A correction is also made for the continual dilution of the fluids. Under these circumstances he finds 10 c.c. Liebig's solution to be equivalent to 0·099 gram urea.

If the urine is too concentrated it is to be diluted, while if it contains much less than 2 per cent. urea the following correction is applied: From the sum of the urea solution and of the soda solution employed in the neutralization, the number of c.c. of mercuric solution employed are to be subtracted; the difference thus obtained multiplied by 0·08 will give the true number of c.c. of the mercuric solution. Suppose 20 c.c. of a urine or a solution of urea containing 1 per cent. require 21 c.c. mercuric nitrate to give the terminal reaction, and that the sodic carbonate solution required for neutralization amounts to 13·95 c.c.; the sum of these = 33·95; subtract from this the 21 c.c. of mercuric nitrate, 33·95 — 21 = 12·95 c.c.; this multiplied by 0·08 = 1·036, or in round numbers 1. If this is taken from the mercuric nitrate, 20 c.c. will represent the corrected amount of mercuric nitrate required.

B. Estimation of Urea by its Conversion into Nitrogen Gas.

This method is founded on the decomposition of the urea by the action of such a body as a hypobromite: $CON_2H_4 + 3NaBrO = CO_2 + N_2 + 2H_2O + 3NaBr$. 1 gram urea contains theoretically 0·4666 gram of nitrogen = 372·7 c.c. In practice, however, when the urea is decomposed by the action of hypobromites, only 354·3 c.c. are obtained. This decomposition method therefore gives results that are about 8 per cent. less than the total nitrogen present. But urine, as we have seen, contains several other nitrogenous constituents, such as urates and kreatinin, which yield up a small proportion of their nitrogen. For ordinary purposes this may be disregarded, but if required these bodies can be separated by precipitation of the kreatinin with an alcoholic solution of chloride of zinc, and the urates by acetate of lead followed by sodic phosphate (Yvon).

The decomposition is generally effected in a graduated tube in which the resulting nitrogen is measured, the carbonic acid evolved being absorbed by the free caustic soda that is always present in the bromine liquor; and it is advisable to reduce the urine to be experimented on as nearly as possible to 1 per cent. urea. If much albumen is present filter the urine after having added a few drops of acetic acid and boiled. Sugar does not materially interfere with the process; but a diabetic urine evolves nearly all the nitrogen of its urea, instead of 8 per cent. less—a fact that should be kept in mind in comparing the results obtained with those given by a non-saccharine urine.

A great many different forms of apparatus have been proposed and recommended, but only three of these will be here described—HÜFNER'S, RUSSELL and WEST'S, and SIMPSON'S.

1. KNOP *and* HÜFNER'S *Method.*—The *bromine liquor* is prepared by placing 70 c.c. caustic soda (about 30 per cent.) in a well-stoppered bottle with 180 c.c. water and 5 c.c. bromine, $2NaHO+Br_2=NaBr+NaBrO+H_2O$. The mixture is well shaken and laid aside, but it spoils by keeping, the hypobromite rapidly changing into the bromate.

Process.—The piece *a b* is first washed out with alcohol and ether and allowed to dry. Then by means of a long pipette the space *a* (including the aperture of the stopcock), which is graduated to contain 5 c.c. as nearly as possible, is to be filled with the urine. The stopcock is then closed, and *b* filled with the hypobromite solution. The upper narrow end of *b* is now to be passed through the cork in the bottom of the shallow dish *c;* into this latter is poured some strong solution of common salt, so as to cover the upper aperture of *b*. The graduated tube *d* is next filled with some of the same salt solution, and inverted over the mouth of *b* and fixed there by means of a clamp. All having been thus prepared, the stopcock is opened, and immediately the hypobromite begins to mix with the urine, and nitrogen gas is evolved and collected in the receiver *d*. The operation is allowed to continue for twenty minutes or so, the apparatus then well agitated, and the receiver *d*, its aperture being closed with the thumb, removed to a vessel filled with water, where it is to be attached to a clamp and lowered till the fluid inside the tube is on the same level as on the outside. Leave for 15 minutes, and having again adjusted the levels read off the amount of gas present.

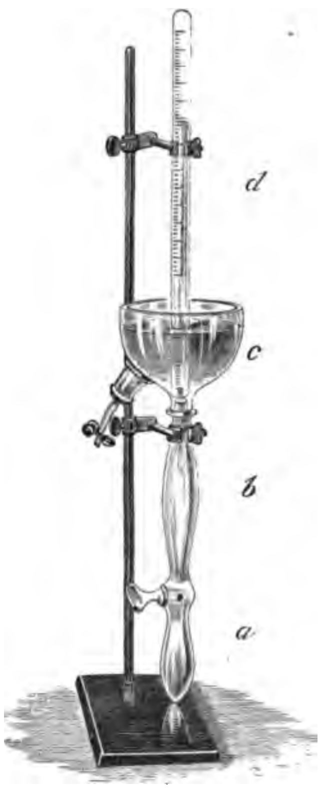


FIG. 30.—HÜFNER'S UREA APPARATUS.

To obtain accurate results the volume obtained must be corrected for temperature and pressure, and for tension of aqueous vapor. The following formula is employed for the purpose:—

$$v^{\circ} = \frac{v(b - w)}{760\ (1 + 0{\cdot}00366t)}$$

v° = required volume.
v = given volume.
b = barometric pressure.
w = tension of aqueous vapor.
t = observed temperature.

This table gives the tensions of aqueous vapor from 10° to 25°:—

10° = 9·126
11° = 9·751
12° = 10·421
13° = 11·130
14° = 11·882
15° = 12·677
16° = 13·519
17° = 14·409
18° = 15·351
19° = 16·345
20° = 17·396
21° = 18·505
22° = 19·675
23° = 20·909
24° = 22·211
25° = 23·582

Example.—30 c.c. gas were obtained at 10° and 750 mm. pressure.

$$v^{\circ} = \frac{30\ (750 - 9{\cdot}126)}{760\ (1 + 0{\cdot}00366 \times 10)} = \frac{30 \times 740{\cdot}874}{760 \times 1{\cdot}0366} = \frac{22226{\cdot}22}{787{\cdot}816}$$

∴ $v^{\circ} = 28{\cdot}2$ c.c.; and as 1 gram urea = 354·3 c.c. nitrogen, therefore (354·3 : 1 = 28·2 : x) $x = 0{\cdot}0792$ gram urea. The amount of urine contained in $a = 5{\cdot}5$ c.c.; accordingly the percentage of the urea is 5·5 : 0·0792 = 100 : x; therefore $x = 1{\cdot}44$ per cent.

II. Russell *and* West's *Apparatus* consists of a decomposing tube 9 inches long and ½ inch wide. At its closed end it is blown into an elongated bulb, which holds about 12 c.c. and is narrowed considerably where the bulb begins. The tube is fixed with its bulb downwards into a metal tray that serves as a pneumatic trough, its mouth being on a level with the bottom of the latter. A plug made of a glass rod with a band of india rubber over one of its ends is fitted so as exactly to fill up the constriction at the mouth of the bulb. The metal tray rests on three long supports, and inside it stands the measuring tube, which is of such a size as to fit over the mouth of the decomposing tube. The measuring tube is so graduated as to save correction for temperature and pressure; it expresses at once the percentage of urea in the 5 c.c. urine experimented on. Further, at a temperature of about 18° a compensation of errors occurs, the tension of the aqueous vapor present with the nitrogen, together with the expansion of the gas itself, nearly counterbalancing the amount of nitrogen not evolved in the reaction.

The authors found that 5 c.c. of a 2 per cent. solution of urea evolved 37·1 c.c. nitrogen at ordinary temperatures and pressures; accordingly 0·1 gram urea corresponds to 37·1 c.c. This volume of gas consequently is taken as representing 2 per cent. of urea, and serves as the basis of the graduation of the tube.

Hypobromite Solution.—Dissolve 100 grams of caustic soda in 250 c.c. of water, and add 25 c.c. of bromine to the solution.

Process.—Measure 5 c.c. of urine into the decomposing tube, wash down the sides of the latter with distilled water so as to fill the bulb, and then insert the plug; the hypobromite solution is next poured into the tube until it is full, and the metal trough half filled with water. When the measuring tube has been filled with water and inverted in the trough, the glass plug is withdrawn and the measuring tube at once brought over the decomposing tube. A torrent of gas arises in bubbles into the former. The reaction is generally completed in 15 minutes, but it may be greatly expedited by warming the bulb gently with a spirit lamp.

5 c.c. normal urine generally evolve about 30 c.c. of gas, but some urines may be much richer in urea and give a proportionately larger volume of gas; if so, it is then advisable to dilute the urine with an equal bulk of water, and to use 5 c.c. of the diluted fluid in the analysis, the volume of gas obtained being doubled in making the calculation.

III. Simpson *and* O'Keefe's *Method*.—The apparatus required consists of a wide-mouthed bottle *a*, $1\frac{1}{2}$ oz. in capacity, having an india rubber stopper with three holes; a bent pipette *b* with its lower end drawn out to a point; a narrow tube *c* about 9 inches long, having its lower extremity pointed and bent upwards, surmounted by a globe and provided with a glass stopcock; a narrow glass delivery tube with a pinch cock at *e*; and a tube *f* graduated like the collecting tube of Russell and West's apparatus.

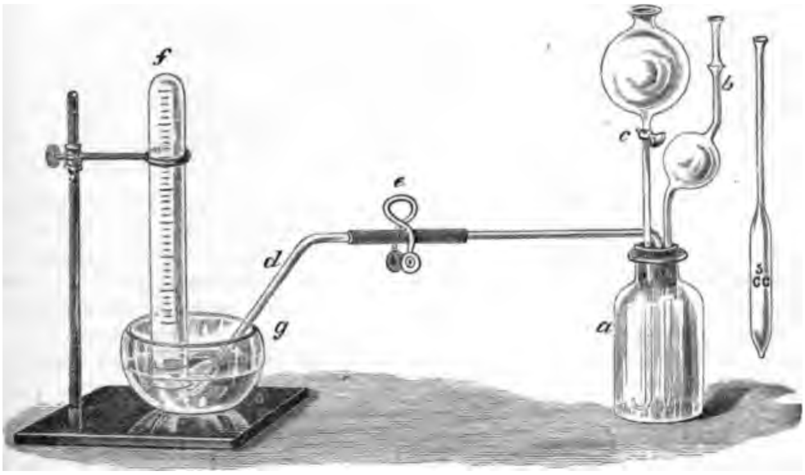


Fig. 31.—Simpson's Urea Apparatus.

To use the apparatus fill the bottle with a solution of hypobromite of soda prepared as in II., and fix in the stopper with its three tubes, taking care to exclude air, and that the ends of the tubes *b* and *c* reach to the bottom; *c* must contain water reaching a few lines higher than the glass cock. The end of the delivery tube *d* is now plunged just below the level of the water in the glass *g*, a little hypobromite solution poured into the pipette *b*, and the pinch cock *e* opened, by which means the air is forced out of the delivery tube. The graduated tube *f* is then filled with water and brought over the end of the delivery tube. The analysis can now be begun by measuring 5 c.c. of the urine into the globe *c*. By turning the stopcock about a third of this is allowed to flow into the hypobromite solution. When all effervescence has ceased the pinch cock is opened and the gas allowed to flow into the graduated tube. The same operation is twice repeated, and then a little water added to wash down all the urine into the bottle. Care must be taken not to let the urine sink below the level of the stopcock before the water is added, and the water in turn should be in sufficient quantity not to sink below the same level. The operation is completed by adding a little more hypobromite to the pipette *b* (into which some hypobromite should always be poured at the beginning of the analysis), and once more opening the pinch cock. Lastly, transfer the graduated tube to a deep vessel containing water, and having brought the water inside and outside the tube to the same level, read off the volume of the gas.

Modifications Proposed.—1. It is said that much better results are obtained by first mixing the solution of urea with caustic soda and then adding the bromine so as to form the hypobromite in presence of the urea. Experimenting in this manner 99·02 to 99·91 per cent. of the whole nitrogen has been obtained (DUGGAN). The soda solution is made by dissolving 20 grams caustic soda in 100 c.c. water, and with every 20 c.c. of this liquid there should be used 1 c.c. bromine. The measuring out of the bromine is facilitated by introducing a few drops of water into the tube containing it, which will float on the top and prevent to a great extent the escape of the bromine vapor.

2. WORMLEY prepares the reagent fresh: 100 grams soda being dissolved in water 250 c.c., and 25 c.c. bromine added when the mixture has cooled; this reagent is to be diluted before use with a volume and a half of pure water, and the urea solution is to be added to the reagent in small portions at a time, all effervescence being allowed to cease before any further addition of the urea; the amount of urea is also not to exceed 1 part to about 1,200 parts of the diluted reagent.

With SIMPSON'S apparatus I have obtained most satisfactory results, particularly with freshly prepared hypobromite solution. C. ARNOLD finds that HÜFNER'S apparatus yields as good results as SIMPSON'S only when the solution contains 1 per cent. of urea; and that, compared with a direct estimation of the urea in urine by soda lime, Hüfner's method yields results 7 per cent. too low, and Liebig's process only 0·5 per cent. too low.

C. Other methods have been employed for the estimation of urea, but only some of these will be referred to, and that in the briefest possible way. (*a*) BUNSEN'S process, which is very accurate, and depends on the decomposition of urea effected by barium chloride at 220°, ammonium carbonate being first formed, which combines with the barium chloride. The carbonate of baryta is insoluble, and can be removed by filtration, dried, and weighed; or dissolved in hydrochloric acid and precipitated from its hot acid solution in the form of sulphate, which is to be washed, dried, heated on platinum foil, and weighed. 233 parts of the sulphate correspond to 60 parts of urea.

(*b*) By the WILL-VARRENTRAP method some of the urine is mixed with caustic soda and heated so as to evolve its nitrogen in the form of ammonia, which is collected in sulphuric acid of known strength. From the loss in acidity, ascertained by titration, the amount of urea is calculated.

(*c*) HEINTZ and RAGSKY determined the urea by heating the urine with strong sulphuric acid, by which means sulphate of ammonia was formed and carbonic acid evolved. The ammonia was then precipitated with platinic chloride, and from the weight of the double chloride formed the ammonia present calculated.

(*d*) By the process of *Nesslerizing* the urea can be determined, 10 c.c. of a 1 per cent. solution of urine being heated to dryness over an oil bath at 150°

in a small retort with caustic potash, and then again after 20 c.c. ammonia-free water have been added to it. The distillate is diluted up to 50 c.c. and then Nesslerized (WANKLYN).

CHAPTER VIII.

URIC ACID.

URIC ACID, $C_5H_4N_4O_3$; molecular weight 168; containing 33·33 per cent. nitrogen.—It exists in the blood as a urate and is separated as such, but a decomposition of this urate occurs in the kidneys or bladder, or more frequently after emission. Normally also it is met with in the spleen, and traces of it have been found in the brain, pancreas, liver, lungs, and heart. It is very rich in the urine of birds and reptiles, in which it replaces urea, but only in small amount in human urine, although occasionally presenting itself as a sandy sediment or orange-colored crystalline powder. Although uric acid can be made by its decomposition to form urea, and may therefore be regarded as a less oxidized product of proteid metabolism, it cannot be regarded as a necessary antecedent of urea; indeed, it would rather seem that its formation is the result of a different metabolism to that which normally results in the production of urea. In the organism of the domestic hen the amido-acids pass into uric acid, as has been established in the cases of leucin and tyrosin (KNIERIEM); and here experiments appear to show that uric acid is not a direct decomposition product of albumen, but rather the result of a synthesis that has its seat probably in the spleen (RANKE). In mammals too it is still doubtful whether the uric acid is a decomposition product preceding urea, although it seems probable that part of it at least is thus derived.

Quantity Excreted.—In the new born the quantity is proportionally greater than in the adult, forming 0·13 per cent. of the urine passed in the first week, then decreasing up to 0·04 per cent., an adult secreting on an average 9¼ to 10½ grs. (RANKE) in the 24 hours, or about 0·03 to 0·05 per cent. of the urine (PARKES). Its excretion is somewhat less in women than in men, but the difference among different individuals, and even in the same individuals is very great. Its amount depends somewhat on the activity of the skin, with profuse perspirations the uric acid diminishing, but when the skin is comparatively inactive, as in winter, the uric acid increasing (FOURCROY).

It is increased by animal food, particularly with insufficient exercise, and diminished by vegetable food. It is also increased by muscular fatigue (RANKE), although active outdoor exercise lessens it. Large doses of quinine and sodic carbonate (SEEGEN) reduce its discharge, as also inhalation of oxygen (ECKART).

Preparation.—(1) Excrement of serpents, Peruvian guano, or uric acid calculi can be used. Powder finely, and after having extracted with dilute hydrochloric acid boil with dilute caustic soda (1 : 20 water) as long as ammonia is evolved; filter hot, dilute, and add some warm hydrochloric acid in excess, or pass a current of carbonic acid to complete neutralization; the uric acid separates as a fine white powder, which is to be well washed with water and dried. By redissolving it in caustic soda and precipitating again with hydrochloric acid it is obtained comparatively pure, when it is to be well washed in water and then dried. The product thus obtained is yellow-colored, but it can be rendered colorless by dissolving it in strong sulphuric acid and then precipitating with water.

(2) To prepare it from human urine add to this one-fifth its volume of hydrochloric acid, which decomposes the urates, lay aside in a cool place, and decant after two or three days; dissolve the deposit of crystals on the walls of the vessel in sulphuric acid, and precipitate with water. As the uric acid is in such small quantity, it is generally advisable to concentrate the urine, particularly if of low specific gravity, to half its volume before adding the hydrochloric acid.

Properties.—Uric acid forms, when pure, a white crystalline powder that is devoid of taste or smell, but when impure it is generally of a yellow or brown color; it is almost insoluble in cold water and only slightly soluble in hot water (1 in 1800), very slightly soluble in alcohol and ether, easily soluble without decomposition in strong sulphuric acid and reprecipitated again on dilution with water; likewise easily soluble in nitric acid, but with attendant decomposition; soluble in caustic soda and potash, but less so in ammonia; soluble likewise in alkaline solutions of lactates, acetates, carbonates, phosphates, and borates forming neutral urates; moderately soluble also in boiling glycerin, but more so in a boiling solution of sodic phosphate.

Under the microscope uric acid is seen to assume a multiplicity of crystalline forms. The *most constant appears to be the rhombic*, frequently with the two obtuse angles rounded. The form is affected by the strength and quantity of the acid added, and by the presence of other bodies (ORD). When precipitated from an alkaline solution by means of hydrochloric acid it forms small transparent rhombic tables, with a few elliptical and oblong plates. Among the forms occurring in urinary deposits the oblong or large hone-shaped form is characteristic.

They may also occur as rhombic prisms or derivatives thereof, or in doubly convex, lozenge-shaped plates, elongated flat plates with excavated ends, rectangular quadrilateral prisms, and dumb-bell-like bundles. The crystals may be separate or arranged in stellate groups. They are nearly always colored. *Indeed, every crystalline urinary deposit of a distinct yellow, brown, or red color may be said to consist of uric acid.* The urine depositing uric acid is also generally high-colored and acid.

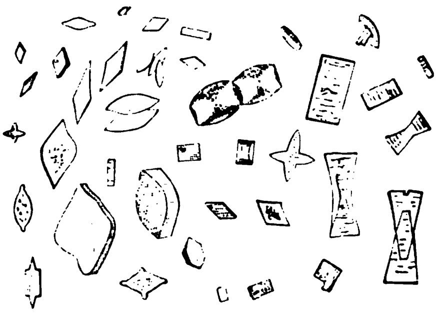


FIG. 32.—CRYSTALS OF URIC ACID.

At *a* are crystals formed by the addition of hydrochloric acid to a solution of uric acid in caustic potash. The rest are different forms of spontaneously separated crystals.

Combinations.—It constitutes a weak dibasic acid, furnishing acid ($C_5MH_3N_4O_3$) and neutral salts ($C_5M_2H_2N_4O_3$); the latter are more soluble than the former. These are a few of its soda salts:—

Urate of sodium . .	$Na_2C_5H_2N_4O_3+H_2O$
Acid " " . .	$2(NaC_5H_3N_4O_3)+H_2O$
Quadriurate " . .	$NaC_5H_3N_4O_3+C_5H_4N_4O_3$.

The acid urates are more permanent than the neutral urates. There are similar urates of potass, ammonia, lithia, and lime. The urate of lithium is the most soluble in water, and that is why salts of lithia are prescribed when an excess of uric acid is supposed to exist in the system; and the sodic urates are more soluble than those of potash or ammonia; the normal also are more soluble than the acid salts. As uric acid is a weak acid its combinations are readily decomposed even by acetic acid, but it possesses the power of decomposing the alkaline phosphates, forming a urate and an acid phosphate.

Decompositions.—These are most interesting as indicating some of the important relationships of uric acid.

1. Uric acid is easily oxidized. By means of potassic permanganate it forms methyl allantoin and carbonic anhydride:

$$C_5H_4N_4O_3+O+2H_2O = C_4H_5(CH_3)N_4O_3+CO_2.$$

2. If the decomposition occurs at a high temperature oxalic acid and urea also appear, while if heated some time with plumbic oxide allantoin, urea, oxalic acid, and carbonic anhydride are formed.

3. Treated with cold nitric acid it furnishes alloxan and urea:

$$C_5H_4N_4O_3+O+H_2O = C_4H_2N_2O_4+CON_2H_4.$$

4. Heated with nitric acid, carbonic anhydride and nitrogen gas are given off, and alloxan, alloxantin, and urea are left behind.

5. By oxidation with alkalies allantoin and carbonic anhydride are formed: $C_5H_4N_4O_3+H_2O+O = C_4H_6N_4O_3+CO_2$. By further hydration allanturic acid and urea are obtained:

$$C_4H_6N_4O_3+H_2O = CON_2H_4+C_3H_4N_2O.$$

In nearly all these decompositions of a molecule of uric acid it will be seen that two molecules of urea and a carbon acid of some kind are formed.

6. Heated in a sealed tube with strong hydrochloric acid it is decomposed into glycocin, carbonic anhydride, and ammonia: $C_5H_4N_4O_3+5H_2O = C_2H_5NO_2+3CO_2+3NH_3$. The converse synthesis of uric acid by fusing together glycocin and urea at a temperature of 200° to 230° has also been effected by HORBACZEWSKI.

7. By reducing uric acid with a weak amalgam of sodium xanthin ($C_5H_4N_4O_2$) and then hypoxanthin ($C_5H_4N_4O$) are obtained.

8. Heated with hydriodic acid to 170° uric acid is decomposed into glycocin, ammonium iodide, and carbonic anhydride:

$$C_5H_4N_4O_3+3HI+5H_2O = C_2H_5NO_2+3NH_4I+3CO_2.$$

• **Tests and Reactions.** 1. *The Murexid Test.*—Place the uric acid in a small porcelain dish, cover it with a few drops of nitric acid, and dissolve with the aid of heat, taking care not to let the temperature rise too high; a yellow or reddish residue is soon obtained, which is to be moistened with a drop of ammonia, when a beautiful *purple red color* appears. The body thus formed is named *purpurate of ammonia* [$C_8H_4(NH_4)N_5O_6$], but it may be observed that the so-called purpuric acid has not been obtained free.

If the uric acid is present in small amount add very little ammonia; it is safer in such a case to expose the residue to its vapor or to use a diluted ammonia (1 to 10). If the residue is treated with caustic potash or soda instead of ammonia a beautiful violet blue color is obtained. The color is dissipated by heat. (Caffein produces a somewhat similar reaction.)

2. Dissolve a little on a glass slide in a few drops of caustic potash with the aid of heat, and add a drop or two of hydrochloric or acetic acid: note the transparent rhombic tables that are formed.

The crystals of uric acid are so varied in shape that when in doubt it is always advisable to treat them as above, and obtain easily recognizable forms.

3. Dissolve a little uric acid in caustic soda, and having added a few drops of Fehling's solution, or of ammonia and dilute cupric sulphate solution, boil: the white cupric urate separates out; after a time it takes a greenish tint. The cupric oxide must not be in excess; otherwise the red cuprous oxide may appear.

4. Dissolve a little uric acid in as little sodic carbonate solution as possible, and, after moistening a piece of filter paper with solution of silver nitrate, by means of a glass rod bring a little uric acid solution down upon the filter paper: a dark spot of reduced silver immediately appears (SCHIFF).

5. If to a little of the solution in the sodic carbonate ammonium chloride is added, a gelatinous precipitate of urate of ammonia is obtained.

6. Add a little solution of uric acid to some sodic hypochlorite in caustic soda: a rosy red coloration is produced, which disappears in excess of the soda (DIETRICH).

To Determine the Presence of Uric Acid in Urine and Ascertain its Amount approximately, etc —1. The presence of uric acid or a urate in an animal fluid may be thus detected: Place the fluid in a watch glass and add a few drops of glacial acetic acid. A few fine filaments of flax or silk are immersed in it, and the whole laid aside under a glass shade for 24 to 48 hours; the filaments are then to be removed and examined microscopically in a little glycerin (GARROD). The separation of the uric acid can be readily effected by boiling the fluid or extract to coagulate any albumen that may be present, then filtering, and evaporating to dryness. The dry residue is to be repeatedly extracted with boiling water, and this extract acidified with acetic acid and laid aside for 24 to 48 hours. In gout the uric acid is generally present in sufficient quantity in the blood to be obtained in the above way in the fluid taken from a blister, but while it accumulates in the body in chronic gout its excretion in the urine diminishes. This is frequently the case in many other diseased conditions in which the uric acid in the urine is diminished; thus in Bright's disease the uric acid in the blood may rise as high as 0·12 to 0·55 (GARROD).

2. In most cases it may be separated by filtering 100 c.c. of the fluid, adding to it 5 c.c. hydrochloric acid, and laying the mixture aside for 24 hours. A deposit of uric acid generally occurs, but the amount cannot be accurately estimated from the quantity of deposit present, although approximative results may be thus obtained.

(*a*) After HEINTZ's *method* 200 c.c. urine are treated with 10 c.c. hydrochloric acid and left in a cool place for 48 hours. The crystals are then collected

on a weighed filter, well washed with cold water, dried some hours between watch glasses, and weighed. Too low a result is generally obtained, but, in order to make up for the loss by the uric acid held in solution, to this should be added 0·0038 gram uric acid for every 100 c.c. of fluid that has been employed.

(*b*) Evaporate one-fourth of the urine passed in the 24 hours to 40 or 50 c.c., having first neutralized it with hydrochloric acid or carbonate of potass as necessary; then add a mixture of hydrochloric acid and alcohol (1 to 4). After the uric acid has been deposited and the supernatant liquid is clear, decant and wash the deposit on a weighed filter first with alcohol, and then with equal parts of acetic acid and water; lastly dry and weigh.

(*c*) A rapid estimation may be made by strongly agitating 200 c.c. urine with 5 c.c. fuming hydrochloric acid for five minutes, and then allowing it to stand aside for an hour. The uric acid that separates is then collected on a weighed double filter, dried at 100°, and weighed. To avoid error from the presence of silica the residue is ignited, and if anything remains it is subtracted from the total weight (A. PETIT).

(*d*) E. LUDWIG thus proceeds: The urine is treated with a combination of ammonio-silver solution and magnesia mixture; and the precipitate, which contains all the uric and phosphoric acids, is filtered off and washed with very dilute ammonia. It is then decomposed by a warm dilute solution of potassic sulphide, forming potassic urate, which passes into solution. The liquid is filtered, the filtrate slightly acidified with hydrochloric acid, and evaporated on the water bath to a small bulk; and the uric acid that separates out on cooling is filtered off, washed with water, and after having been dried at 110° treated with bisulphide of carbon to free it from adhering sulphur, and then with ether.

Pathology. *Occurrence of a Deposit.*—Healthy urine may deposit uric acid 10 to 20 hours after emission, and such deposition is a normal event during the so-called acid fermentation period, but a deposit occurring three or four hours after the urine has been passed is not normal. This early deposit may be seen in convalescence from febrile complaints, especially articular rheumatism; also in chorea, some forms of diabetes, enlarged spleen, and in the middle periods of Bright's disease (ROBERTS). Lessened respiratory power of the blood is probably one of the great factors in increasing the excretion of uric acid.

Uric acid is increased in the urine after attacks of indigestion, in acute dropsies, in inflammations such as pneumonia, and acute rheumatism in the stage of congestion and exudation, and in some skin diseases (especially eczema and lepra); frequently also it is increased in leukæmia, paroxysms of intermittent fever, and generally in all disturbances of the circulation and respiration, as in emphysema, etc. In phthisis 9·8 grains, in acute hepatitis with jaundice 11·18 grains, in cases of jaundice 17·75 grains, and in milk fever 19 grains have been passed in the 24 hours (BECQUEREL).

It is diminished in chronic maladies in general, except during their periods of exacerbation; also in the later stages of Bright's disease, in diabetes, in cases of polyuria, and in gouty affections; likewise in anæmic conditions, chronic rheumatism, paraplegia, and chronic diseases of the spinal cord.

CHAPTER IX.

URATES AND URIC ACID DERIVATIVES.

URATES are commonly found in urinary sediments, calculi, or arthritic deposits. 8·69 per cent. cases of calculi contain urates as nuclei, while in 16·08 per cent. layers of urates are present (THUDICHUM).

These urates appear to differ considerably in composition, the bases varying, but usually consisting of soda, ammonia, potash, and lime. Uric acid has been found to form 80 to 90 per cent. of their weight.

Uric acid	94·00
Potash	3·15
Ammonia	1·36
Soda	1·11

(Bence Jones).

But some authorities regard the urate of soda as constituting the chief component of urinary deposits.

Properties.—They occur generally in the form of an amorphous yellow, brown, or red-colored powder, occasionally mixed with fine colorless needles, the color being due to urinary pigment. The urates dissolve in boiling water, and are deposited when the water cools. The urates of soda and ammonia are sometimes deposited in the crystalline form; in gouty concretions, for example, the urate of soda is found in the form of delicate needles forming bundles of stars, or lying separately. The *urate of soda* is occasionally found in the urine of gout, and in febrile conditions, particularly in children. It appears as an amorphous powder or as minute spherules armed with little prisms. In dilute solutions, after a time, the last forms may appear as short hexagonal prisms or thick tables. The urate of potash closely resembles the sodic urate in its properties. *Urate of ammonia* in the crystalline condition most frequently assumes the form of dark spheres and globular masses, although sometimes appearing as minute, slender, and imperfectly formed dumb-bells.

Solutions of urates are readily decomposed by hydrochloric acid, uric acid being precipitated.

Heated on platinum foil with a drop of caustic potash urate of ammonia gives off ammonia, recognized by the smell, while urate of soda leaves a residue of sodic carbonate that is alkaline and effervesces with hydrochloric acid.

They show the murexid reaction.

Solutions of alkaline urates give a white precipitate with salts of lead, a green precipitate with cupric sulphate, a violet with chloride of gold, and a yellow with silver nitrate. Any urinary deposit that disappears on the application of heat consists of urates. They are more frequently colored than white. The deposit is bulky and amorphous, but containing minute spheres with protruding spicules.

A *urate deposit may occur* after much loss of water by sweating and violent exercise, or after prolonged abstinence from food and drink; it is often present in the urine of persons who eat much meat and drink little water (Scherer), and also during functional derangements of the digestive organs, particularly in cold weather.

URIC ACID DERIVATIVES.

Alloxantin ($C_8H_4N_4O_7+3H_2O$) is obtained from uric acid by the action of very dilute nitric acid, and can easily be prepared by mixing together the concentrated solutions of alloxan (142 grams) and dialuric acid (144 grams)-

It forms rhombic tables and columns, and gives a temporary blue coloration with ammonia and ferric chloride. Silver nitrate is reduced by it, and with baryta water it forms a characteristic violet precipitate, which loses its color when heated, decomposing into dialuric acid and baric alloxanate. Saturated with dry ammonia gas at 100°, it is decomposed into water and murexid: $C_8H_4N_4O_7+2NH_3 = \underset{\text{(murexid.)}}{C_8H_8N_6O_6}+H_2O$.

The most important *derivatives* of alloxantin are alloxan, murexid, uramil, dialuric, oxaluric ($C_3H_4N_2O_4$), parabanic, and barbituric ($C_4H_4N_2O_3$) acids.

Alloxan ($C_4H_2N_2O_4$) is obtained when uric acid is dissolved in nitric acid (specific gravity 1·41) at a low temperature, separating out of a saturated solution as a white crystalline deposit:

$$C_5H_4N_4O_3+H_2O+O = C_4H_2N_2O_4+CO(NH_2)_2.$$

To *prepare it* stir up alloxantin with very strong sulphuric acid, so as to form a thick mud, and after this has stood for several days spread it out to dry in the air; then evaporate to complete dryness over a water bath and crystallize out of hot water.

It forms large rhombic pyramids or small monoclinic crystals. A saturated watery solution when rapidly boiled is decomposed:

$$\underset{\text{(alloxan.)}}{3(C_4N_2H_2N_4)} = \underset{\text{(alloxantin.)}}{C_8N_4H_4O_7}+\underset{\text{(parabanic acid.)}}{C_3N_2H_2O_3}+CO_2.$$

When boiled with a strong alkali it is also decomposed:

$$\underset{\text{(alloxan.)}}{C_4N_2H_2O_4}+2H_2O = \underset{\text{(mesoxalic acid.)}}{C_3H_2O_5}+\underset{\text{(urea.)}}{CON_2H_4}.$$

Boiling dilute nitric acid changes alloxan into parabanic acid and CO_2:

$$C_4N_2H_2O_4+O = C_3N_2H_2O_3+CO_2.$$

Dilute sulphuric and hydrochloric acids decompose it into alloxantin, urea, and oxalic acid; when heated with peroxide of lead urea and CO_2 are obtained; and reducing agents develop dialuric acid: $C_4H_2N_2O_4+H_2 = C_4H_4N_2H_4$.

Uramil ($C_4H_5N_3O_3$) is *prepared* by heating a cold saturated watery solution of thionurate of ammonia $[C_4H_3(NH_4)_2N_3SO_6+H_2O]$, adding a little hydrochloric acid, boiling some minutes, and collecting the crystalline deposit of fine needles on cooling. The thionurate is obtained by passing a current of sulphurous acid for some time into a cold saturated solution of alloxan, then adding ammonium carbonate and boiling for half an hour. On cooling the thionurate separates. It is to be washed, dissolved in hot water, the boiling solution precipitated with acetate of lead, and the thionurate of lead collected, washed, suspended in cold water, and decomposed with hydric sulphide. The filtrate is concentrated at 140° to a small bulk until crystals begin to separate.

Purpuric Acid and Murexid.—The acid is not known in the free state, but it exists in murexid, which is the acid purpurate of ammonia. The *murexid* can be obtained by the electrolysis of alloxan, by heating ammonium dialurate, by the action of ammonium carbonate on warm solution of alloxantin or alloxan, by heating dry alloxantin at 100° with ammonia gas, and by evaporating a solution of uric acid in nitric acid and heating the residue with ammonia:

$$C_5H_4N_4O_3+H_2O+O = \underset{\text{(alloxan.)}}{C_4H_2N_2O_4}+CO(NH_2)_2;$$

$$3C_4N_2H_2O_4 = \underset{\text{(alloxantin.)}}{C_8N_4H_4O_7}+\underset{\text{(parabanic acid.)}}{C_3N_2H_2O_3}+CO_2;$$

$$C_8N_4H_4O_7+2NH_3 = \underset{\text{(murexid.)}}{C_8H_8N_6O_6}+H_2O.$$

Murexid can be best *prepared* by heating uramil (4) and mercuric oxide (1) in water (30), adding a few drops of ammonia, heating gently up to boiling point, and, after boiling a few minutes, filtering.

Murexid forms four-sided tables or columns that are of a red garnet hue with transmitted and a metallic green with reflected light. Its solution in boiling water has a purple tint; in alcohol and ether it is insoluble. When warmed with acids it decomposes into uramil, alloxan, and ammonia, and the alloxan still further into alloxantin and urea.

Parabanic Acid, $C_3H_2N_2O_3$.—It is prepared by rapidly transferring uric acid (1 part) in small portions at a time to 6 parts nitric acid (specific gravity 1·3) heated up to 70°. When effervescence has ceased the solution is evaporated to a syrupy consistence at the same temperature. On cooling crystals separate, which are to be collected on a filter and dissolved in hot water (1½ part), from which pure parabanic acid is deposited.

It forms thin, colorless, six-sided prisms, and its solution gives a white granular precipitate with silver nitrate, which is soluble in ammonia: $C_3Ag_2N_2O_3 + H_2O$.

Allantoin ($C_4H_6N_4O_3$).—This body is found in the human allantoic fluid and in the urine of young sucking calves; it occurs in very small amount in normal human urine, particularly in that of a new-born child for the first few weeks after birth, during pregnancy (GUSSEROW), and after the ingestion of tannic acid. It has also been found in the urine of dogs after the administration of uric acid (SALKOWSKI), and in respiratory obstruction (FRERICHS). It is generally abundant in the urine of cats. In the placenta of both dogs and cats crystals of allantoin are found, often associated with hæmatoidin and occasionally hæmoglobin crystals, and also biliverdin.

It is *prepared* by rubbing up uric acid (3) with water, and adding to it potassic permanganate (1), taking care not to let the temperature rise; filter rapidly, and having saturated the filtrate with acetic acid, leave aside 24 hours to crystallize. Its derivation from uric acid may be thus expressed:

$$C_5H_4N_4O_3 + O + H_2O = C_4H_6N_4O_3 + CO_2.$$

It also may be obtained by evaporating allantoic fluid, the crystals being washed in water, and their solution in hot water decolorized with animal charcoal.

To separate it from urine precipitate with lead acetate, filter, and, having passed hydric sulphide through the filtrate, evaporate it to a syrup and let it stand for several days. The crystalline mass is to be washed in cold and dissolved in hot water, from which the allantoin is allowed to separate.

It crystallizes in small, colorless, glistening prisms, and is slightly soluble in cold and more soluble in hot water, but insoluble in cold alcohol and ether. Its solutions are neutral, giving no precipitate with mercuric chloride, but a precipitate with mercuric nitrate $[2(C_4N_4H_5O_6)_2.Hg + 3HgO]$; silver nitrate also gives a white crystalline precipitate. It is decomposed by concentrated alkalies:

$$3(C_4H_6N_4O_3) + 13H_2O = 12NH_3 + 6CO_2 + 2(C_2H_2O_4) + C_2H_4O_2.$$

CHAPTER X.

HIPPURIC ACID.

HIPPURIC ACID, $C_9H_9NO_3$, may be regarded as benzoyl glycocin, $C_2H_4(C_7H_5O)NO_2$, a glycocin in which an atom of hydrogen is displaced by the radical benzoyl $C_6H_5.CO$.

It is a more important constituent of the urine of herbivora than of carnivora, though it exists in considerable amount in animals living on a mixed diet. It is probably present in combination with one of the alkalies.

Origin and Amount.—It arises in part from the oxidation of albumens, and in part also from such acids as the benzoic and cinnamic, etc., when absorbed. A vegetable diet, and particularly fruit like greengages, blackberries, and plums, which contain benzoic acid, increase its amount in the urine; the use of different balsams also has a similar effect.

In the urine of different individuals it averages from 0·02 to 0·06 per cent. In starvation its elimination does not appear to be affected, for in a case where the urea excreted amounted only to 6·6 grams and the uric acid to 0·07 gram the hippuric acid was 1·16 gram. Occasionally its discharge undergoes a great increase, and BOUCHARDAT has described such a condition under the name *hippuria.*

Benzoic acid, when ingested, is changed in the liver, kidneys, or alimentary canal into hippuric acid. But this power of changing benzoic into hippuric acid seems to be reduced in certain affections of the kidney, such as amyloid degeneration and acute and chronic inflammations. Occasionally in jaundice hippuric acid has not been found even after the administration of benzoic acid.

In some cases of diabetes it is increased, but in others it has been noticed to be diminished, and in icterus and some kidney affections it is diminished.

It has been met with in the sweat also, especially after the use of benzoic acid and certain balsams.

LEHMANN was of opinion that the increased acidity of the urine of fevers was due to this body, but recent investigations are opposed to this idea.

Preparation.—1. Boil the fresh urine of a horse or cow for some minutes with milk of lime in excess to remove the pigment, filter the hot fluid, and evaporate rapidly to $\frac{1}{10}$ its volume; when cold, acidulate with hydrochloric acid. After 24 hours decant the fluid from the deposited brownish yellow crystals; dissolve them up again in boiling milk of lime, filter, to the hot filtrate add hydrochloric acid, and crystallize as before. The crystals may be rendered colorless by the action of animal charcoal or by heating their solution in excess of caustic soda with potassic permanganate solution, adding this body drop by drop to the boiling liquid until a little of the solution, when filtered, gives a pure white precipitate with hydrochloric acid. The whole fluid is then filtered and supersaturated with hydrochloric acid.

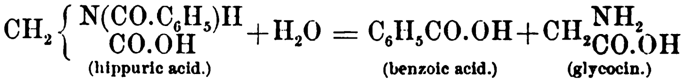
2. Treat the fresh urine with zinc sulphate, evaporate to one-sixth the volume, filter, and decompose the zinc hippurate with hydrochloric acid, and separate the hippuric acid by crystallization.

3. *To obtain it from human urine* give 30 grams benzoic acid to a patient in the evening, and the next morning collect his urine. Evaporate it to a small volume, and when it has cooled treat it with hydrochloric acid and lay it aside in a cool place. After some hours the deposit is collected on a filter and washed with cold water and alcohol. The crystals thus obtained may be purified still further as in the first method.

Properties.—Hippuric acid forms brilliant hard white and translucent four-sided rhombic prisms or needles, generally taking the form of prisms when deposited from a dilute, and of needles from a saturated, solution. The crystals are moderately soluble in hot water, and easily soluble in alcohol and benzol, the solutions having an acid reaction; soluble also in sodic phosphate, and in alkalies and their carbonates; but almost insoluble in ether and chloroform. Hippuric acid reduces an alkaline solution of cupric sulphate.

It is monobasic and forms neutral salts that are generally soluble in water and crystallizable, the iron hippurate alone being amorphous.

Derivatives.—When boiled with strong mineral acids and alkalies it is split up into benzoic acid and glycocin :



$$CH_2\left\{\begin{matrix}N(CO.C_6H_5)H\\CO.OH\end{matrix}\right.+H_2O = C_6H_5CO.OH+CH_2\begin{matrix}NH_2\\CO.OH\end{matrix}$$

(hippuric acid.) (benzoic acid.) (glycocin.)

Ferments produce the same effect; and a watery solution of hippuric acid to which sodic phosphate has been added, after a few days at a temperature of about 30°, undergoes a similar change.

Heated strongly in a small tube it gives a sublimate of benzoic acid and ammonium benzoate, evolving, at the same time, an odor of new hay or bitter almonds, hydrocyanic acid and benzo-nitril being formed, and oily red drops deposited in the tube.

Tests.—1. Boil a little hippuric acid with a few drops of nitric acid, evaporate to dryness, and heat the residue in a small tube or porcelain capsule: an intense odor of nitro-benzene is evolved. Benzoic acid gives the same odor; but hippuric is distinguished from benzoic acid by its insolubility in ether and its non-volatilization on being heated, also by the shape of its crystals.

2. Boil a little with strong hydrochloric acid, and the hippuric acid will break up into benzoic acid and glycocin. Add an excess of caustic potash and a drop of cupric sulphate solution, and a deep blue coloration is produced, not destroyed by boiling: this is due to the glycocin.

3. *To Detect in Urine.*—(*a*) Treat the urine with chloride and milk of lime to separate the phosphates, neutralize the filtrate with hydrochloric acid, and treat with nearly neutral ferric chloride, when a brown hippurate is thrown down. By neutralizing with sodic carbonate before filtration, then filtering, washing, and boiling the precipitate with alcohol, the hippurate may be removed, and by heating this with hydrochloric acid hippuric acid can be separated.

(*b*) Evaporate a litre of urine almost to dryness; rub up the residue with baric sulphate, acidify with hydrochloric acid, and exhaust completely with alcohol; neutralize the alcoholic extract, distil off the alcohol, and having added a little oxalic acid evaporate to dryness. Exhaust the dry mass with ether to which some alcohol has been added, and evaporate the ethereal solution. Treat the residue with warm milk of lime, filter, and evaporate the filtrate to a small volume, which is finally to be acidified with hydrochloric acid. The hippuric acid crystallizes out.

HIPPURIC ACID DERIVATIVES—BENZOIC ACID AND GLYCOCIN.

BENZOIC ACID, $C_7H_6O_2 = C_6H_5COOH$.—This body exists ready formed in several balsams and resins, particularly gum benzoin, and is found in the urine of the herbivora as a consequence of hippuric acid fermentation. It is occasionally met with also in the smegma præputii, sweat and suprarenal capsules; but it does not appear normally to be preformed in the organism.

It can be *produced* by boiling a watery solution of hippuric acid with strong hydrochloric acid for an hour:

$$\underset{\text{(hippuric acid.)}}{C_2H_4(C_7H_5O)NO_2} + H_2O = \underset{\text{(glycocin.)}}{C_2H_5NO_2} + \underset{\text{(benzoic acid.)}}{C_7H_6O_2}.$$

Properties.—Benzoic acid volatilizes without decomposition at 240°, and is deposited in the form of fine elongated needles or thin, flexible, pearly plates. When ingested it passes out in the urine as hippuric acid. It dissolves readily in alcohol, ether and ammonia, but only to a slight extent in boiling water. Perchloride of iron gives with benzoic acid or alkaline benzoates a brown precipitate of benzoate of iron. Solutions of free benzoic acid or its salts with the alkalies are not precipitated by a mixture of alcohol, ammonia, and baric chloride, thus differing from succinic acid, which is thereby precipitated.

Derivatives.—If benzoic acid is moistened with nitric acid and evaporated in a small capsule it will give off the smell of nitro-benzol. Heated to redness with the caustic alkalies it evolves carbonic acid and benzol. When acted on with sodium amalgam a solution of benzoic acid yields benzyl alcohol, $C_6H_5.CH_2.OH$.

By the distillation of ammonium benzoate with phosphoric anhydride a colorless oily fluid is obtained, benzonitril, $C_6H_5.CN$.

GLYCOCIN (*Glycocol*, *Glycin*), $C_2H_5NO_2 = CH_2NH_2COOH$, crystallizes in large rhombohedra which are soluble in water, but insoluble in cold alcohol and ether. It is a decomposition product formed by the action of acids or alkalies upon such animal substances as glue, gelatin, fibrin, and hippuric acid; obtained also by the decomposition of glycocholic acid by boiling it with hydrochloric acid:

$$\underset{\text{(hippuric acid.)}}{C_9H_9NO_3} + H_2O = \underset{\text{(glycin.)}}{C_2H_5NO_2} + \underset{\text{(benzoic acid.)}}{C_7H_6O_2}.$$

It may be regarded as amido-acetic acid, as it is built up by the action of ammonia upon chloracetic acid:

$$\begin{matrix}CH_2Cl\\COOH\end{matrix} + 2NH_3 = \begin{matrix}CH_2NH_2\\COOH\end{matrix} + NH_2Cl.$$

It appears to be allied to the cyanogen compounds, and a substitution glycocin is sarcosin or methyl glycocin.

Glycocin is not found preformed in the organism, although some regard it as a constituent of the liver; but it can easily be formed there by the decomposition of such bodies as albumen and gelatin, a change that probably occurs in the liver; for when benzoic acid is injected into the portal vein it is excreted by the urine as hippuric acid, but when rapidly injected into the jugular vein it passes into the urine unchanged (KÜHNE). It is probable, however, that the conversion is not effected solely in the liver, but that the kidneys also assist (SHEPPARD). In the duodenum also it is possible that a similar decomposition occurs under the action of the pancreatic juice.

Preparation.—Boil impure hippuric acid for an hour with four times its weight of strong hydrochloric acid, and then evaporate nearly to dryness. Extract the residue with a little water, boil this watery extract for a few minutes with freshly precipitated hydrated plumbic oxide, and separate the precipitated plumbic chloride by filtration; pass hydric sulphide through the filtrate to complete the separation of the lead; this final filtrate contains the glycocin, and is to be evaporated to a small bulk till crystallization sets in.

Also obtained by the action of acids or alkalies on gelatin.

Derivatives.—Under the action of nitrous acid glycocin is changed into glycocollic acid ($C_2H_4O_3$), water and nitrogen being evolved at the same time. When heated with baryta it is decomposed into carbonic anhydride and methylamin:

$$\underset{\text{(glycocin.)}}{CH_2.NH_2.COOH} + Ba(OH)_2 = \underset{\text{(methylamin.)}}{NH_2CH_3} + BaCO_3 + H_2O.$$

Ammonic permanganate in an ammoniacal solution oxidizes it, there being formed carbonic acid, oxalic acid, oxamil ($CO.NH_2.COOH$), carbamic acid, and water.

CHAPTER XI.

KREATININ.

Of the remaining organic constituents we cannot do more here than refer to a few, such as kreatinin, indican, and the urinary pigments.

KREATININ, $C_4H_7N_3O$ or $N_2\left\{\begin{array}{l}CN\\CH_3\\H_2\\(C_2H_2O)''\end{array}\right.$

This is a constant constitutent of urine. It forms brilliant colorless, oblique, rhombic prisms, and is supposed to be derived from the kreatin of muscle, as it is simply a dehydrated form of that body. An alkaline solution of kreatinin, for example, left to itself for some time changes into kreatin.

Amount.—A grown man excretes in the 24 hours 0·5 to 1·3 gram, or a mean of one gram (Hofmann). Women excrete a little less than men; infants on a pure milk diet excrete little or none; boys (10 to 12 years) excrete a mean of 0·387 gram, and old people a mean of 0·5 to 0·6 gram. Its proportion is increased by a rich flesh diet and diminished by abstinence.

Pathologically it is increased in acute febrile processes, as typhus, pneumonia, and intermittent fever, and diminished during the convalescence of the same (Munk), being also lessened in anæmia, chlorosis, diabetes, chronic Bright's disease, and tetanus.

Preparation. 1. *From Kreatin.*—It can easily be prepared by evaporating to dryness a mixture of kreatin (1), water (3), and sulphuric acid (1), then boiling the residue with freshly precipitated baric carbonate to separate the acid, filtering and evaporating; or by boiling the kreatin for half an hour with dilute hydrochloric acid, adding hydrated plumbic oxide, filtering, evaporating the filtrate to dryness, extracting the residue with alcohol and again evaporating: kreatinin crystallizes out in colorless prisms.

2. *From Urine.*—Evaporate 15 to 20 pints of urine to one-fourth to one-eighth its volume, and having allowed it to cool decant from the precipitated salts, add acetate of lead to the decanted liquid, and filter. The excess of lead in the filtrate is then removed by a current of hydric sulphide, or by the addition of sodic carbonate; filter again, nearly neutralize, and add a strong solution of mercuric chloride, which causes a precipitate of kreatinin in combination with itself. This precipitate is suspended in water, decomposed with

a current of hydric sulphide, filtered, the filtrate decolorized with animal charcoal, and then evaporated to dryness. Kreatinin hydrochloride remains. It is to be crystallized two or three times from strong spirit, and the hydrochloric acid separated from it by boiling with hydrate of lead (MALY).

Properties.—It forms colorless, glistening, rhombic columns, easily soluble in hot water and alcohol. It acts as a strong alkali, coloring litmus paper blue, and being capable of displacing ammonia from its combinations, forming also double salts with some of the metals and salts with the acids.

Combinations.—It combines with hydrochloric acid ($C_4H_7N_3O + HCl$), a watery solution of this body after the addition of sodic acetate giving a precipitate with chloride of zinc. With platinic chloride and hydrochloric acid it forms a double salt that is crystalline and of an orange red color. With chloride of zinc a granular crystalline precipitate [$(C_4H_7N_3O)_2ZnCl_2$] separates when a strong solution of the chloride of zinc is added to a moderately strong solution of kreatinin. By using an alcoholic solution the separation is rendered more complete. This kreatinin zinc chloride is converted into kreatin by boiling its solution with hydrated oxide of lead.

Characteristics and Tests.—1. Add to a dilute solution some drops of a very watery solution of *sodium nitroprusside*, then drop by drop a little dilute caustic soda: a beautiful ruby red color shows itself, which soon disappears (WEYL). This test may be applied to the urine directly. If the reaction does not appear, boil the urine first with dilute sulphuric acid.

2. Add *zinc chloride* to a strong watery or alcoholic solution of kreatinin, and a heavy crystalline powder is thrown down, which is soluble in hot water and acids, and insoluble in alcohol. With pure solutions the crystals are in the form of fine needles arranged in bundles or rosettes, or as little balls.

This reaction may be employed to *estimate the kreatinin quantitatively*: Precipitate the phosphates in 250 c.c. urine with milk of lime and then with calcic chloride; filter in a couple of hours, and evaporate the filtrate to a syrupy consistence; treat this with 50 c.c. absolute alcohol, and having thoroughly mixed it transfer to a small beaker, and let it stand for 6 to 8 hours. To the filtrate add 10 to 15 drops of an alcoholic solution of chloride of zinc. After 2 or 3 days bring the precipitate upon a weighed filter, and wash it there with alcohol (90 per cent.); then dry and weigh: 100 kreatinin zinc chloride = 62·42 kreatinin.

If the urine contains albumen this should first be separated. Sugar should also be removed by fermentation. Any kreatin can be converted into kreatinin by boiling the urine for half an hour with sulphuric acid.

3. When warmed with *Fehling's solution* it reduces the cupric salt.

4. Acidified with nitric acid and heated with a dilute solution of *phosphomolybdic acid* it gives a yellow crystalline precipitate, consisting of four-sided crystalline plates that are soluble in hot nitric acid.

5. *Nitrate of silver* gives a white crystalline precipitate, easily soluble in boiling water; *mercuric chloride*, a white caseous flocculent precipitate which quickly changes to a mass of fine needles; *mercuric nitrate* with sodic carbonate also precipitates it.

CHAPTER XII.

THE URINARY PIGMENTS.

What these are is still a subject of controversy; indeed, whether there is but one pigment or several it is as yet difficult to say. In certain abnormal conditions, however, it is very probable that there are really more than one. The whole question, it must be confessed, is so far in an unsettled condition.

As SCHUNCK has shown, these urinary pigments are very readily decomposed, which may possibly account for many of the pigments described as normal constituents of the urine.

Urobilin, looked upon as identical with hydrobilirubin, is regarded by many authorities as the chief urinary pigment. On the other hand THUDICHUM has described a pigment (*urochrome*) which he regards as a derivative of hæmoglobin, and as constituting the chief normal urinary pigment.

But, in addition to these, other pigments have been enumerated. HELLER'S *uroxanthin* appears to be identical with *indican* (SCHUNCK), a body frequently present in urine, particularly under disordered conditions of the system. The body described as *uroerythrin* is found chiefly in connection with such urinary deposits, particularly of fevers, as uric acid and urate of soda. It is probably equivalent to PROUT'S *purpurate of ammonia* and GOLDING BIRD'S *purpurin.* But there is some reason to believe that there are at least two of these pigments, one soluble and the other insoluble in chloroform. In certain leprous affections bodies giving absorption spectra, and named *urorubrohæmatin* and *urofuscohæmatin,* have been described as existing (BAUMSTARK). In melanotic cancer a chromogen may occasionally be met with which blackens on exposure to the air. Also after the use of carbolic acid a dark brown pigment of the nature of a hydrochinon derivative appears in the urine.

MACMUNN states that normal urine contains a body apparently identical with choletelin, and he thinks that all the coloring matters of bile, including hæmatin, are oxidized to choletelin. The urobilin of bile is produced in the intestine, and in certain states of the system may appear in the urine, but normally it is oxidized to choletelin. While most of the urinary pigments may be traced back to the bile pigments some of them may be directly derived from hæmatin, and these latter may sometimes replace the former.

UROBILIN (*Hydrobilirubin*), $C_{32}H_{44}N_4O_7$.—In the urine of fevers, and then in normal urine, JAFFÉ found a pigment which is especially characterized by certain absorption bands in the spectrum, and by a green fluorescence when an ammoniacal solution is treated with chloride of zinc. HOPPE SEYLER, however, is of opinion that normal urine does not contain urobilin, but rather a compound that is precipitated by plumbic acetate, which, when decomposed by sulphuric acid and alcohol, yields little by little urobilin in consequence of spontaneous oxidation. This urobilin is recognized spectroscopically in only about 10 per cent. of normal urines, but after treatment with hydrochloric, sulphuric, or nitric acid most urines show the characteristic band between *b* and F. Also by treating the urine with neutral and then with basic lead acetate, and digesting the precipitate with alcohol acidulated with sulphuric acid, it is possible to obtain an extract giving the same absorption band, although with the urine of fevers such treatment is seldom necessary. If the extract thus obtained is shaken up with water and chloroform, and the chloroform extract decanted and evaporated, the urobilin will remain behind as a coffee brown, oily, neutral mass. MALY maintains that the hydrobilirubin he gets by acting on bilirubin with sodium amalgam is identical with JAFFÉ'S urobilin; HOPPE SEYLER also regards as of the same nature the body obtained by the reducing action of tin and hydrochloric acid on hæmoglobin and hæmatin; and LIEBERMANN states that the continued reduction of choletelin produces a similar substance. This hydrobilirubin JAFFÉ supposes to have its origin in the intestine as the result of the action upon the bilirubin of the bile of the nascent hydrogen generated as a consequence of many of the intestinal decompositions. And as the bilirubin is probably built up in the liver at the expense of the hæmoglobin of the blood corpuscles, the globulin constituent furnishing the biliary acids (HOPPE SEYLER), the urinary pigment would thus have its primary source in the breaking down of the colored corpuscles of the blood. The hydrobilirubin, when formed, would be absorbed as such and excreted as the coloring matter of the urine.

Preparation of Hydrobilirubin. 1. *From Bilirubin (after* MALY).—Suspend the bilirubin in water and digest it with sodium amalgam for some days in a small flask loosely closed, warming occasionally. The amalgam slowly dissolves, generating hydrogen; the nascent gas reduces the bilirubin, which dissolves up in the caustic soda that gradually forms:

$$2C_{16}H_{18}N_2O_3 + H_2 + H_2O = C_{32}H_{40}N_4O_7.$$

The color of the solution gets less and less, and when no further change occurs decant the supernatant fluid from the deposited mercury and acidulate it with hydrochloric or acetic acid, which precipitates the greater part of the hydrobilirubin in brown flocculi. These are then to be collected on a filter, washed with water, dissolved up in ammonia, and reprecipitated with hydrochloric acid. The hydrobilirubin still remaining in solution in the filtrate is to be separated by adding to it zinc sulphate and then ammonia; this precipitate is also to be carefully washed.

2. *Of Urobilin from Urine.*—Highly colored urine of fevers (10 to 30 litres) is rendered alkaline with ammonia, filtered, and the filtrate precipitated with chloride of zinc. The precipitate is washed with cold and then with hot water, boiled with alcohol, and dried at a gentle heat. The dried precipitate is powdered, dissolved in ammonia, and precipitated with neutral lead acetate. To the red-colored precipitate some oxalic or sulphuric acid is added, and after it has been rubbed up with alcohol and let stand aside for 24 hours it is to be filtered. The acid alcoholic filtrate shows the absorption bands of urobilin as well as a green fluorescence when it is rendered alkaline with ammonia and a drop of zinc chloride solution added. The alcoholic solution is finally to be shaken up with its own volume of chloroform and rather more than this of water, when the chloroform takes up the urobilin. The chloroform solution is now to be separated by decantation, shaken up once again with water, and the chloroform removed by distillation. An amorphous resinous precipitate is obtained.

Properties.—Urobilin is not crystalline, but forms hard, reddish brown masses with a greenish tint by reflected light. It is insoluble in water, but easily soluble in alkalies, alcohol, chloroform, and ether, forming rosy red solutions that exhibit a green fluorescence, and with suitable dilution an absorption band between *b* and F. Its solution in alkalies is brownish, but it becomes yellow on dilution. Unlike bilirubin it gives no color reaction with nitric acid; but its ammoniacal solution, when largely diluted and zinc chloride added, gives an evident green fluorescence.

Detection of Urobilin.—1. Urine of fevers as well as urines that have stood some time frequently show a green fluorescence and the characteristic absorption spectrum after having been rendered strongly alkaline with ammonia, filtered, and a few drops of zinc chloride solution added to the filtrate. If this is not obtained directly, shake 50 to 100 c.c. of the urine with an equal volume of pure ether; dilute the decanted ethereal solution, and dissolve up the residue in a few c.c. of absolute alcohol. The alcoholic solution has generally a yellow tinge, is fluorescent, and gives the absorption spectrum. In icteric urine urobilin is abundant, and can be obtained from it after the bile pigments have been separated by milk of lime and carbonic acid.

2. Precipitate 200 c.c. urine with basic acetate of lead, filter, and after having washed the precipitate with water dry it at a gentle heat; then rub it up with strong spirit, adding a little oxalic or sulphuric acid; lay aside for twenty-four hours and filter. The filtrate is fluorescent and shows the absorption band when rendered alkaline with ammonia and treated with chloride of zinc. These appearances, however, may be better seen with the extract obtained by shaking the alcoholic filtrate with water and chloroform. Shake a little of the chloroform extract with some iodine solution and dilute caustic potash: a yellow to a brownish yellow coloration is obtained with marked greenish fluorescence (GERHARDT).

There are many urines that at first give no absorption spectrum, but which after a time become darker colored and exhibit it distinctly; but the same urines may be made to show the characteristic reaction, without such delay, by treating them with acetate of lead and decomposing the precipitate by means of an acid. This leads one to suppose that the urobilin is not always present as such, but may exist as an uncolored body, urobilinogen or urochromogen—an opinion, we have seen, HOPPE SEYLER holds with regard to normal urine.

3. Urobilin can easily be detected in the fæces by extracting with alcohol and examining the alcoholic extract as in 1 or 2.

UROCHROME (THUDICHUM) is an amorphous dark yellow colored substance, soluble in water and less soluble in alcohol, ether, dilute acids, and alkalies. It is decomposed by dilute acids, and when boiled with them its decomposition products consist of a mixture of uromelanin, uropittin, and omicholin. Its watery solutions are precipitated by silver nitrate, acetate of lead, and acetate and nitrate of mercury.

Uromelanin has the formula $C_{36}H_{43}N_7O_{10}$ (THUDICHUM), showing a close correspondence to that of the choroidal pigment.

Preparation.—Acidify the urine with sulphuric acid, and precipitate it completely with nitric acid solution of phosphomolybdic acid; wash the precipitate with water slightly acidulated with sulphuric acid, and decompose it with boiling baryta water in excess; filter and free the filtrate from baryta by a current of carbonic acid gas. Precipitate successively with neutral and basic lead acetate and with ammonia; collect the precipitates and decompose them with hydric sulphide.

Or the lead precipitates may be decomposed with sulphuric acid, and the filtrate precipitated with phosphomolybdic acid.

The urochrome is purified by shaking its aqueous solution with a little freshly precipitated oxide of silver.

This body, about which considerable doubt is still expressed, has repeatedly been prepared by the author according to the different processes proposed by THUDICHUM. He has also verified many of THUDICHUM'S statements as to its character and properties, and has convinced himself as to its non-identity with hydrobilirubin.

CHAPTER XIII.

INDICAN.

INDICAN (*Uroxanthin*) belongs to the indigo series, which is nearly related to the benzene group. In certain plants of the genus Indigofera a glucoside exists called indican, $C_{26}H_{31}NO_{17}$; this body under the influence of acids or ferments generates indigo blue and indiglucin, $C_{26}H_{31}NO_{17} + 2H_2O = C_8H_5NO + 3C_6H_{10}O_6$. SCHUNCK regarded the indican that sometimes occurs in urine as of the same nature as the indican of plants; but BAUMANN and others affirm that the indican of urine is not a glucoside, as it yields no body capable of reducing cupric salts (indiglucin, $C_6H_{10}O_6$), but, instead, probably an ether of the same, oxindol sulphuric acid, and accordingly it is not identical with the indican of plants. BAUMANN assigns to the *indican of urine* the formula $KC_8H_6NSO_4$, as he considers it indoxyl potassic sulphate. It is probably equivalent to HELLER'S uroxanthin; the formula $C_8H_7NSO_4$ has accordingly been taken as representative of the composition of the acid, which, however, is not known in the free state. The liver is supposed to be the seat of its formation, and JAFFÉ looks upon its appearance in the urine as the result of the presence of indol in the alimentary canal. When indol (C_8H_7N) is taken in the food or injected subcutaneously the indican in the urine is increased. Indol is a constituent of the fæces, being probably formed by the continued action of the pancreatic secretion upon albumen (NENCKI). This indol is oxidized in the organism and combines with sulphuric acid, the change possibly taking place in the intestine. The greater part of the indol is eliminated by the fæces, communicating to these their characteristic odor, but part is absorbed and appears in the urine as indican. In intestinal obstruction, therefore, it should be greatly increased in the urine, and JAFFÉ has found this to be the case. If finely powdered indigo is mixed with the food of rabbits the urine will precipitate indigo blue on the addition of hydrochloric acid; but this does not hold good with dogs.

Many urines, when strongly acidified with hydrochloric acid, become blue-colored and deposit a blue pigment; and often when a urine containing indican becomes putrid the indican decomposes, indigo white and then indigo blue being formed, a blue pellicle appearing on the surface of the urine. Occasionally also it appears in the sweat.

Preparation. (*a*) *Of Indigo from Urine of Horse.*—Concentrate to a syrup, and extract with excess of alcohol; then distil off the alcohol and shake the residue with several times its volume of ether. The syrup now remaining is to be separated from the uric acid crystals with which it is mixed and dissolved in water; this solution is treated with neutral and then with basic acetate of lead so long as a precipitate is formed, and to the filtrate some acetate of lead and ammonia added, and the whole laid aside for 24 hours. The precipitate then formed is collected, and after it has been expressed it is suspended in water and a current of carbonic acid passed through. The filtrate from this is evaporated to dryness, the residue extracted with alcohol, and a current of hydric sulphide passed to separate any lead that may be present. The final filtrate then obtained is evaporated to dryness, but the product is impure.

The filtrate also from the normal and basic lead acetate may be precipitated with ammonia, and the precipitate collected, washed, and decomposed with fuming hydrochloric acid. From the filtrate indigo blue separates, generally mixed with some lead chloride.

Dog's urine, which is very rich in indican, may be used instead of horse's urine. Even on boiling it with hydrochloric acid it is possible to obtain the indigo as a fine powder.

(*b*) *From Indigo.*—In the following process the purification is effected by first reducing the crude indigo to indigo white, and then reoxidizing the latter. Reduce some finely powdered indigo (3 parts) with slaked lime (6 parts), ferrous sulphate (4 parts), mixing them together with boiling water (450 parts), and filling a flask completely with the mixture; cork tightly and lay aside till a deep yellow solution is obtained; indigo white or indigogen is formed ($C_{16}H_{12}N_2O_2$). Now transfer the fluid by means of a syphon to a vessel containing dilute hydrochloric acid: a precipitate is obtained, particularly after the whole has been well shaken, the indigo white having oxidized into indigo blue or indigotin: $C_{16}H_{12}N_2O_2+O=C_{16}H_{10}N_2O_2+H_2O$. If little or no exposure to the air has occurred, the yellow liquid will give a precipitate of indigo white on the addition of the hydrochloric acid; but this body absorbs oxygen with great avidity.

Cautious sublimation of commercial indigo gives nearly pure indigo blue. The sublimation is best effected by mixing powdered indigo (1) with plaster of Paris (2), making into a paste with water, and then drying upon an iron plate. Heat this mass over a spirit lamp, and minute irregular crystals of pure indigo will appear on the surface. When these crystals are sublimed they rise as a fine blue or violet red vapor, that condenses into dark blue needles having a coppery lustre. These are insoluble in water, alcohol, ether, and dilute acids and alkalies, but easily soluble in boiling chloroform or amyl alcohol.

Quantity of Indican.—Normal urine is poor in indican; it gives no colored chloroform solution if previously treated with an equal volume of hydrochloric acid. As a mean JAFFÉ found 6·6 milligrams in 1,000 c.c., but it appears to be abundant in the urine of inhabitants of the tropics. Horse's urine contains 152 milligrams in 1,000 c.c. Feeding dogs with gelatin did not increase the indican, while a corresponding amount of flesh raised it to 16 to 17 milligrams per day. The quantity of indican, however, is very variable, and the same may be said for its indications. In cases of cancer of the stomach and liver HOPPE SEYLER some days found much indigo, but only traces on others.

Tests.—1. Mix 20 to 40 drops urine with 3 or 4 c.c. fuming hydrochloric acid; or the urine may be warmed after the addition of a little hydrochloric or nitric acid; a violet red or intense blue color is developed. Sometimes the addition of 2 or 3 drops concentrated nitric acid favors the reaction (HELLER).

2. Mix equal volumes of the urine and of hydrochloric acid, and add cautiously, drop by drop, a saturated solution of chloride of lime, shaking well until a green color makes its appearance; if much indican is present a red, violet, or blue color will develop, and a blue deposit may be obtained on filtration (JAFFÉ). Normal urine generally gives a reddish violet color when thus treated. SENATOR recommends the addition of chloroform after the chloride of lime; when the whole is then well shaken the chloroform dissolves up the indigo blue formed and sinks to the bottom of the vessel as a blue solution which gives an absorption band in the spectrum between C and D (STOKVIS). Ether can be employed instead of the chloroform, and a dilute solution of bromine water in place of the lime chloride solution, which does not keep well. The reaction can also frequently be obtained by the addition of $\frac{1}{6}$ the volume of the urine of hydrochloric acid followed by the chloroform alone. If the urine contains albumen this must be separated before applying the test, while an excess of pigment may be removed by lead acetate.

3. Warm the urine with twice its volume of nitric acid, and shake with a little chloroform and ether: if indigo blue is present a violet blue solution will be obtained, giving the absorption band. Or the same result will be obtained by the addition of some hydrochloric acid containing a trace of nitric acid, and subsequently shaking the mixture up with a little chloroform.

Quantitative Estimation. I. *Approximative.*—The quantity may be approximately estimated by adding 5 c.c. hydrochloric acid to 20 or 30 drops of urine, warming gently without boiling, and agitating constantly. Dark striæ form and the color soon becomes a very pale violet, a darker violet, or a pale or dark blue. Now add 2 drops nitric acid and warm gently: the blue and violet tints disappear and a more or less intense yellow tint makes its appearance—very slowly when the indican is abundant, but rapidly when it is scanty. The indican is *diminished or absent* when no change, or only a pale violet tinge, is attained; evidently *present* when the violet color is marked; *abundant* when it is of a distinct blue; *very abundant* when there is produced immediately a blackish pulverulent precipitate.

II. *Quantitative* (SALKOWSKI).—(1) *To prepare the standard solution of indigo blue* bring some finely powdered indigo blue upon a filter and weigh it between watch glasses. Then pour some hot chloroform repeatedly upon the filter, and after drying the filter between the watch glasses weigh it again: the loss in weight will give the amount of indigo blue dissolved in the chloroform. About 200 c.c. chloroform may be employed for the purpose. (2) Take two small beakers and place 10 c.c. urine and 10 c.c. hydrochloric acid in each. Add to the one (*a*) 0·2 c.c. and to the other (*b*) 0·4 c.c. filtered solution of chloride of lime (1 : 20). After half a minute or so note the change of color—*b* is generally darker in tint. To *a* add 0·4 c.c. more, and to *b* the same; note the color about 30 seconds or so after each addition, and continue adding more until the tint becomes no darker, but rather brighter from destruction of the indigo. Suppose that to effect this 1·2 c.c. have been added, then we may regard 1 c.c. as sufficient for our estimation.

(3) Now take 10 c.c. urine, 10 c.c. hydrochloric acid, and 1 c.c. chloride of lime solution, and mix them together. This is to be neutralized with caustic soda, saturated to excess with carbonate of soda, thrown on a small filter, and washed thoroughly with hot water till the alkaline reaction has disappeared; the filter is next dried, cut into pieces, and heated in a small flask with chloroform until the color is completely removed from the filter paper. The same is also to be done with the urine prepared as in (2). For urines moderately rich in indican about 30 c.c. chloroform are required, but for urines rich in this body much more is necessary. Accordingly, to save the chloroform only 2·5 or 5 c.c. of the urine may be originally employed instead of 10 c.c., this being made up to 10 c.c. with water. (4) Filter the chloroform extract into a dry cylinder, and dilute up to a round number with chloroform.

(5) It is next necessary to determine the intensity of color, and for this purpose we should be provided with two little flattened glass chambers, whose walls are about 1 cm. apart. These may be fixed on the same plate of glass. To the one add 10 c.c. chloroform extract, and to the other 10 c.c. chloroform. Into the latter drop from a small burette as much indigo solution of known strength as will impart the same intensity of blue as that of the chloroform extract. Place the little vessels on white paper.

10 c.c. urine gave 30 c.c. blue-colored chloroform extract. 10 c.c. pure chloroform required an addition of 20 c.c. of the standard indigo solution to attain the same intensity of color. The indigo solution contains in 200 c.c 0·0074 gram indigo; therefore 20 contain 0·00074; accordingly the 10 c.c. of urine from which the chloroform extract was obtained contain 0·00074 gram indigo, and 100 = 0·0074 gram.

Derivatives.—Indican combines with the metals, forming salts that are not decomposed by acetic acid, but readily so by the stronger acids even in a dilute form; under their influence it splits up, sulphuric acid separating and indigo blue being generated. Concentrated hydrochloric acid, to every 100 c.c. of which 2 drops chloride of lime solution (1 : 20) have been added, serves this purpose admirably. It is thus resolved into sulphuric acid and oxindol, the latter passing readily into indigo blue:

$$2C_8H_6NKSO_4 = C_{16}H_{10}N_2O_2 \text{ (indigo blue)} + 2KHSO_4.$$

By the action of concentrated acids a purple red sublimable body, probably identical with HELLER'S *urrhodin* and SCHUNCK'S *indigrubin*, is obtained, which is insoluble in water, but forms a carmine red solution in alcohol and ether. Many urines are especially rich in this urrhodin.

Indigo Blue (C_8H_5NO) forms minute irregular crystals; it is insoluble in water, alcohol, ether, and dilute acids and alkalies, but easily soluble in boiling chloroform or amyl alcohol, the solution in this last reagent giving an absorption band. It dissolves in strong sulphuric acid, forming a blue solution, and if to a weak solution of indigo blue in sulphuric acid soda and then sodic sulphate are added, *indigo carmine* [$C_{16}H_{18}N_2O_2(SO_3K)_2$] is generated, which shows a dark absorption band between C and D of the spectrum.

Indigo blue when heated with strong reducing agents, as by distillation over heated zinc dust, etc., generates oxindol, and finally indol. *Indigo white* (C_8H_5NO or $C_{16}H_{10}N_2O_2$) is one of its first reduction products. This *indol* (C_8H_7N) is one of the decomposition products of albuminous bodies, and it is possibly also one of the results of the continued pancreatic digestion of such bodies (NENCKI), although its appearance is more probably due to a simultaneous putrefaction; for no indol makes its appearance if salicylic acid is present. Indol is readily prepared by decomposing albumen with the caustic alkalies; also in small quantity by heating albumen in water up to 200° under pressure. It crystallizes from its solutions in hot water in shining colorless laminæ, and when fused with potash it is converted into anilin; potassic nitrite added to its solution acidulated with HCl gives a rosy red coloration, and a deal shaving that has been dipped in hydrochloric acid is stained a deep red by its vapor, or when dipped in its solution; with picric acid it forms a crystalline compound.

Skatol (C_9H_9N—NENCKI and BRIEGER) is another product of the putrefactive changes occurring in the intestine which may be here just passingly referred to. When present in the urine it gives a violet red color with strong hydrochloric acid and chloride of lime (BRIEGER), and is soluble in water and ether. When a mixture of finely divided muscle and pancreas is allowed to putrefy, and then distilled after the addition of acetic acid, skatol distils over. It can next be precipitated with picric acid, and the precipitate distilled with ammonia (NENCKI).

By suspending some finely powdered indigo blue in boiling water (3), and gradually adding to it nitric acid (sp. gr. 1·3), the blue color disappears, and from the filtrate when cold *isatin* separates. This last body can be dissolved up again in caustic potash, reprecipitated with hydrochloric acid, and crystallized from alcohol, from which it is deposited in brilliant reddish yellow prisms. After the ingestion of isatin the urine is altered to a red or black color, and gives a dark red granular precipitate that is insoluble in water, but soluble in alcohol and acetic acid.

The *continued reduction of isatin* produces the following bodies:—

(Isatin = $C_{16}H_{10}N_2O_4$)
Isatyd = $C_{16}H_{12}N_2O_4$
Dioxindol = $C_{16}H_{14}N_2O_4$
Oxindol = $C_{16}H_{14}N_2O_2$
Indol = $C_{16}H_{14}N_2$.

When boiled with strong caustic potash it is decomposed into anilin, hydrogen, and carbonic anhydride. Strong nitric acid, when boiled with it, gives nitrosalicylic acid, and if the oxidation is continued picric acid, $C_6H_2(NO_2)_3OH$.

Indigo forms two sulphates with boiling sulphuric acid—indigo-monosulphonic acid ($C_{16}H_9N_2O_2.SO_3H$), and sulphindigotic acid, $C_{16}H_8N_2O_2(SO_3H)_2$. Crude indigo, when boiled in succession with dilute acetic acid, yields *indigo gelatin;* with dilute caustic potash, *indigo brown;* with alcohol, *indigo red;* leaving a residue of nearly pure indigo blue.

CHAPTER XIV.

ADDITIONAL ORGANIC CONSTITUENTS.

I. Phenol Sulphonic Acid, $C_6H_5.SO_4H$.—In the 24 hours only about 0.001 gram is excreted in the urine; but this may be increased to three times that amount with a rich vegetable diet, or after ingestion of phenol or benzol; and a pathological increase shows itself in peritonitis, particularly in ileus and lympho-sarcomatous tumor in the abdominal cavity. 0·17 to 0·23 or even 0·34 gram in the 24 hours has been observed.

It can be *prepared* from horse's urine by evaporating it to a small bulk, extracting this with alcohol, and evaporating the extract to a syrup, which is to be laid aside in a cold place to crystallize. The deposit is collected and dried between folds of filter paper and then recrystallized from boiling spirit. Potassic phenolsulphonate $\left(\left.\begin{matrix}C_6H_5\\ K\end{matrix}\right\} SO_4\right)$ is thus obtained, forming white pearly scales.

If rapidly heated it melts, and dissolves easily in water; the solution gives a ruby red color with ferric chloride.

II. **Cressol Sulphonic Acid,** $C_6H_4(CH_3)SO_4H$.—In human urine this is present in only very small proportion, while in the urine of the herbivora it is comparatively abundant; accordingly its amount is affected by the diet.

The potassic salt of this body closely resembles that of the previous acid. When treated with hydrochloric acid it is decomposed into sulphonic acid and paracressol, an oily body distilling at 197° and forming colorless prisms at a low temperature.

III. **Brenzcatechin Sulphonic Acid** is another occasional constituent of human urine. Its presence is usually indicated by the urine containing it becoming dark-colored when decomposition is setting in. The dark brown coloration shows itself first in the surface layers; when treated now with alkalies it soon becomes of a brownish black.

This body reduces ammoniacal solutions of silver and mercuric nitrate, and alkaline solutions of cupric sulphate. It can be separated from a urine containing it with acetate of lead, which does not precipitate grape sugar.

Hydrochloric acid decomposes this acid into sulphuric acid and brenzcatechin [$C_6H_4(OH)_2$], a body apparently identical with **BOEDECKER's** *alkapton*. This brenzcatechin reduces auric, argentic, and cupric salts; its alkaline solution, when exposed to the air, absorbs oxygen, and takes a greenish and then a brownish black color. Its watery solution gives a smalt green with ferric chloride, or a violet after the addition of acetic acid and ammonia.

The administration of pyrogallic acid [$C_6H_3(OH)_3$], salicin ($C_{13}H_{18}O_7$), hydroquinon and resorcin [$C_6H_4(OH)_2$] causes an increase in the amount of brenzcatechin sulphonic acid.

IV. **Kryptophanic Acid** ($C_5H_9NO_5$) has been described by THUDICHUM as the normal free acid of the urine. He regards it as a tetrabasic body that unites freely with the metals, forming salts, and he obtains it therefrom as a transparent, gummy, solid body, whose aqueous solutions are precipitated by silver and mercuric nitrates.

MALY, PIRCHER, and SALKOWSKI, however, have found it, and accordingly they regard it as a variable mixture of still unknown bodies.

V. **Nephrozymase** is a body described by BÉCHAMP as occurring in normal urine, and which is precipitated from that fluid by the addition of three times its volume of alcohol. It is a protein substance, according to him, which between 60° and 70° forms sugar; but LEUBE regards it as a mixture of an albuminous and of a saccharine body.

VI. In the urine of old people *Alcohol* is always present in small proportion.

CHAPTER XV.

THE INORGANIC CONSTITUENTS OF URINE.

THESE, as we have seen, consist chiefly of the bases sodium, potassium, ammonium, calcium, magnesium, and iron combined with hydrochloric, phosphoric, and sulphuric acids, together with gases and traces of nitrates. The sodium exists mainly as chloride. The bases, as well as their amount, depend largely on the nature of the food; if the food is deficient in salts, so also will be the urine. With a vegetable diet the excess of the alkalies in the food reappears in the urine, and with an animal diet the earthy bases predominate.

CHLORIDES.—Chloride of sodium is one of the most essential of the saline constituents of the organism. It is contained in all its tissues and secretions, and its presence excites assimilation, as well as being indispensable for the formation of most of the secretions, and particularly of the gastric juice.

It crystallizes in the cubic system, but when the crystals form in a solution containing organic substances it appears in the form of octahedra as well as in cubes; sometimes it is met with in the urine crystallized in combination with urea in the form of rhombic plates ($CON_2H_4,NaCl+H_2O$).

A saturated watery solution contains at ordinary temperatures 31·84 per cent. of the salt. It is almost insoluble in absolute alcohol. A *standard solution* can be readily prepared by adding an excess of the salt to water, agitating frequently, and filtering after twenty-four hours. 10 c.c. of this solution contain exactly 3·184 grams NaCl; and 20 c.c. are diluted with water up to 318·4 c.c., of which 10 c.c. = 0·2, or 200 milligrams of NaCl.

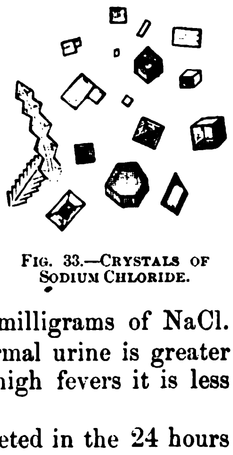


FIG. 33.—CRYSTALS OF SODIUM CHLORIDE.

Amount.—The proportion of chlorides in normal urine is greater than that of all the other salts together; only in high fevers it is less than the sum of the sulphates and phosphates.

In *male adults* the proportion of chlorine excreted in the 24 hours = 6 to 10 grams (NaCl = 10 to 16 grams), or a mean of 7 grams chlorine (108 grains) and 11·5 grams sodium chloride (178 grains), or 0·126 gram per kilo. of body weight; in *adult females* a mean of 5·5 to 6·5 grams chlorine, or 0·116 per kilo.; and for *children* above 3 years 4·5 to 5·3 grams chlorine. HEGAR places the average about 11 to 15 grams, though he says it may vary between 7·4 and 13 grams; VOGEL gives it as 10 to 13 grams.

The amount undoubtedly varies in different individuals, and varies even on different days in the same person, sometimes as much as 30 to 60 per cent., depending on the nature and amount of the food, being increased some hours after a meal, salt beef and copious ingestion of fluids particularly augmenting it; but, as BARRAL has shown, the whole of the sodic chloride in the food is not excreted as such, about a fifth of it being decomposed by acid potassic phosphate to form potassic chloride and acid sodic phosphate. Mental and physical activity also increase it, and it is more abundant during pregnancy. RÖHMANN is of opinion that the organic albumen in becoming circulating albumen binds sodium chloride with itself, and that this is liberated in the decomposition of the albumen.

Tests.—1. *Silver nitrate* produces a white precipitate of silver chloride which is insoluble in nitric and hydrochloric acids, readily soluble in ammonia, and blackens on exposure to the light.

2. *Mercurous nitrate* gives a white precipitate (calomel) which is insoluble in water and blackened by ammonia. Both these tests can be applied to the urine.

3. A solution of a chloride gives a white precipitate of plumbic chloride on the addition of *neutral plumbic acetate*, which is soluble in boiling water.

4. *Strong sulphuric acid* added to the dry salt causes hydrochloric acid gas to be evolved.

5. Sodic chloride imparts an intense yellow color to the flame, giving the well-marked double line D in the spectrum.

Pathological Alterations.—In estimating the chlorides it must be remembered that part of them is to be reckoned as potassic chloride. SALKOWSKI indeed believes that the amount of the potassic chloride is increased during febrile affections, even to three to five times its ordinary amount, after the crisis its quantity returning to the normal. A fever patient therefore excretes more potash than soda, the convalescent more soda than potash. ZÜLZER has shown that with the diminution in the excretion of phosphoric acid in fever there is also a diminished excretion of sodium chloride, whilst the potassium chloride is correspondingly increased. RÖHMANN'S experiments indicate that in fever less sodic chloride is excreted than is ingested, which would point to a retention of the salt in the economy. But the character of the food in fevers must have an influence on the amount of potassic chloride in the urine, coffee, beef tea, and beer, etc., being rich in potash salts. The sodic chloride seems to be required in inflammatory exudations, effusions, or other exudations. Proliferations (as in cancer) and different fluxes or discharges cause it to disappear in whole or in part from the urine. In all acute fevers, particularly those in which there are abundant exudations, new formations, or fluxes, there is likewise a notable diminution in the chlorides excreted. In these cases not merely is the ingestion of the salt lessened, but it is kept back in the body. In pneumonia, for example, towards the crisis the sodic chloride may be absent from the urine: thus in a case of croupous pneumonia during the fever there was a daily excretion of 1 to 1·6 gram; the day after the crisis, 7·87 grams; and the second day, 16·18 grams. That it is not diminished entirely on account of its excretion elsewhere in exudation is seen by its diminution in such diseases as typhus, recurrent fever, etc. In most chronic diseases also the chlorides are likewise lessened in the urine, as is the case often in Bright's disease, rickets, chorea, and pemphigus; and they are absent in cholera.

In the early days after the crisis of fevers the chlorides are *increased;* also after the absorption of exudations and transudations, and occasionally in prurigo and diabetes. In diseased conditions an increase in the elimination of chlorine may be generally regarded as a favorable sign.

Volumetric Determination of Chloride of Sodium in Urine.

I. LIEBIG'S *Process.*—This process, though very interesting theoretically, cannot be recommended, some authorities even regarding it as comparatively useless (HABEL and FERNHOLTZ).

A solution of urea gives a precipitate with a solution of mercuric nitrate, but no precipitate with mercuric chloride. Now if mercuric nitrate is added to a solution of the sodium chloride, double decomposition occurs ($Hg2NO_3+2NaCl=HgCl_2+2NaNO_3$) and mercuric chloride is formed; so that if urea also were present it would not be precipitated by the mercuric nitrate until all the sodic chloride had been decomposed. Upon this fact **Liebig's** process is based. A weak solution of mercuric nitrate of known strength is added to the solution of sodic chloride, which also contains some urea, until a permanent turbidity is produced, slight opalescence that disappears on shaking being disregarded. The urea here acts as the indicator of the termination of the reaction.

Preparation of the Mercurial Solution.—The solution must be as free as possible from traces of other metals, such as bismuth or lead, as these would produce a cloudiness in the liquid while being titrated, and thus interfere with the exact ending of the reaction being readily recognized. Pure mercury must therefore be employed, or, what will be better, pure red mercuric oxide. 18·42 grams of this oxide are placed in a beaker with sufficient nitric acid to dissolve the oxide with the aid of a gentle heat, and when a clear solution is obtained it is evaporated to a syrupy consistence to expel excess of free acid. It is next diluted with water, and if the preliminary operations have been properly carried out a yellow precipitate of basic nitrate of mercury will be deposited, which must be allowed to settle; the clear supernatant liquid is poured off, and a few drops of nitric acid added to the precipitate to redissolve it. An excess of acid must be carefully guarded against, as it would materially interfere with the accuracy of the titration. The two fluids are then mixed and the solution *graduated.* 10 c.c. of the standard sodium chloride are poured into a beaker, and to this 3 c.c. of a 4 per cent. solution of urea and 5 c.c of saturated solution of sodic sulphate are added. The mercuric solution is now allowed to drop slowly into this mixture, the fluids being agitated with a glass rod, and the addition continued until a permanent precipitate is formed, any temporary opalescence being disregarded. If now, to produce this result, say 7 c.c. of the mercurial solution were required, it is too strong and must be diluted with its own volume of water. Let the solution thus diluted be again titrated; and suppose 14 c.c. are required by the 10 c.c. of the sodic chloride solution to form a permanent precipitate, then to every 140 c.c. of the mercurial solution 60 c.c. of water must be added, so as to obtain a solution of which 20 c.c. shall be equal to 10 c.c. of the standard sodium chloride solution, and 100 c.c. exactly indicate 1 gram NaCl, or 1 c.c. = 0·01 or 10 milligrams.

Before the urine can be titrated the phosphoric acid present in it, which would precipitate the mercuric nitrate, *must be removed.* This is done by the addition of a *baryta mixture* thus prepared:—

Saturated solution of barium nitrate . . .	1 volume.
Baryta water (saturated)	2 volumes.

Process.—100 c.c. of the urine are mixed with 50 c.c. of the baryta mixture, well shaken, and filtered. As the filtrate is alkaline it must first be *carefully* acidulated with a few drops of nitric acid, and 15 c.c. (= 10 c.c. urine) are taken and titrated with the mercuric solution.

If the urine contains albumen this must first be removed by boiling the urine after it has been acidified with acetic acid.

II. **Mohr's** *Process.*—To this process also there are many objections in the case of urine, particularly when the chloride is present in small amount, as in the urine of fevers; but it serves very well when the chlorides are abundant.

If nitrate of silver is added to a solution containing sodic chloride, neutral chromate of potash, and an alkaline phosphate, the chlorides will first be precipitated, then the chromate, and lastly the phosphate, the production of a red coloration (due to the formation of chromate of silver) indicating the completion of the precipitation of the chloride. This process of **Mohr's** has been applied by **Neubauer** to the volumetric analysis of chlorides in urine, neutral potassic chromate being used as the indicator.

1. *Standard Silver Nitrate.*—Dissolve 29·075 grams fused nitrate of silver in 1,000 c.c. distilled water: 1 c.c. = 0·01 NaCl.

2. *Saturated Solution of Neutral Potassic Chromate.*

Process.—10 c.c. urine are diluted with 100 c.c. distilled water, and a few drops of potassic chromate added. The silver solution is now allowed to drop in slowly until the appearance of a trace of orange indicates the end of the reaction.

Only in cases where the urine is not highly colored can it be titrated *directly* as above. An excess of the silver solution is required, as the urine contains certain compounds more readily precipitable than the chromate; accordingly 1 c.c. should be subtracted from the total number of c.c. of the silver solution used before making the calculation. But if the urine is high colored, or at all decomposed, or contains excess of uric acid, mucus, or albumen, one of the following processes is to be adopted so as first to *remove these organic compounds*:—

1. Measure 10 c.c. of the urine into a platinum capsule, add to this 1 to 2 grams pure nitre, evaporate to dryness, and then heat the residue carefully till the ash appears white; allow to cool, dissolve up the ash in water, and filter; acidulate the filtrate with dilute nitric acid, and having neutralized with carbonate of lime, add 2 or 3 drops of the potassic chromate and titrate with the silver solution.

2. Boil 10 c.c. of the urine with 5 c.c. of potassic permanganate solution (3·16 grams per litre), filter, and titrate as before. The precipitate consists of organic matter and manganous salt, and enough permanganate should be used to give a slight rose tint to the filtrate: this is removed before titration by the addition of a few drops of solution of oxalic acid.

III. FOLHARD'S *Method as Modified by* SALKOWSKI.—This is the most accurate process for the quantitative estimation of chlorides in urine.

Principle.—If a little nitrate of silver solution is acidified with nitric acid. and some rhodium ammonio-chloride added, a white flocculent precipitate is thrown down; while if an iron salt, such as iron ammonia alum, is also present, a red color will appear immediately the whole of the silver has been precipitated. Now, if the rhodium solution is of known strength, the amount of silver present can be readily calculated. Accordingly, if this method is employed in the estimation of chlorides, an excess of a titrated silver solution is added, and the amount of this excess determined by the rhodium solution.

Preparation of Solutions. 1. *Silver Solution.*—Dissolve in distilled water pure fused nitrate of silver 29·075 grams and make up to a litre. 1 c.c. = 0·01 gram NaCl.

2. *Iron Solution.*—Make a cold saturated solution of iron ammonia alum. This salt should be free from chlorides; if not, purify it by crystallization.

3. *Rhodium Solution.*—The strength of the solution should be such that 25 c.c. = 10 c.c. silver solution. Make a watery solution of commercial rhodium ammonio-chloride, about 6·5 to 7 grams in 1,100 c.c. water.

Dilute 10 c.c. of the silver solution to 100 c.c. with distilled water, add 4 c.c. pure nitric acid and 5 c.c. of the iron solution. Then titrate this mixture with the rhodium solution till a faint permanent red coloration is produced. If, say, only 23·8 c.c. instead of 25 have been required we must dilute accordingly: $23.8 : 25 = 1000 : x$. $x = 1050·4$. Therefore 50·4 c.c. water must be added to the litre.

Process.—10 c.c. urine are placed in a small glass-stoppered flask, graduated so as to contain 100 c.c. up to a mark in the neck. Add 50 c.c. water and then 4 c.c. pure nitric acid (1·2 specific gravity). Now pour in 15 c.c. silver solution and shake vigorously until the precipitate settles. Next make up to the mark with distilled water and filter the contents of the flask into a dry test glass or a small flask which has a mark on its neck indicating 80 c.c. capacity. The 80 c.c. of filtrate are to be poured into a beaker of about 250 c.c. capacity, 5 c.c. iron solution added, and the mixture titrated with the rhodium solution until the first trace of a *permanent* blood red coloration appears.

Let us suppose that 6·8 c.c. rhodium solution have been required for 80 c.c. of the filtrate, therefore 8·5 c.c. for 100 (80 : 100 = 6·8 : 8·5). Now the 15 c.c. silver solution added to the urine are equivalent to 37·5 rhodium solution (10 : 15 = 25 : 37·5); but only 8·5 have been required; therefore 37·5 —8·5 = 29 c.c. correspond to the silver solution that has combined with the chloride, and 29 c.c. are equivalent to 11·6 silver solution (25 : 10 = 29 : 11·6). 1 c.c. silver solution = 0·01 NaCl; therefore 11·6 = 0·116 NaCl. As only 10 c.c. urine were employed, this would give a percentage of 1.16 NaCl.

The percentage is readily obtained by the following formula, which will easily be comprehended from the preceding calculation:—

$$\{37{\cdot}5 - (\text{rhodium solution required in c.c.} \times \tfrac{5}{4})\} \times \tfrac{4}{100}.$$

IV. C. Arnold, so as to obviate any difficulty in noting the end of the reaction by means of the red coloration of the iron, first treats the urine with an equal volume of baryta mixture (see under I.), and adds to 10 c.c. of the filtrate, or even to 10 c.c. of the urine direct, as many drops of nitric acid as are necessary to give a strong acid reaction, then 2 c.c. of the iron solution and 3 or 4 drops of permanganate of potash solution (1 : 30). The silver solution is next added in excess, the whole made up to 100 c.c., thrown on a dry filter, and 50 c.c. of the filtrate titrated with the rhodium solution as in III. to determine the excess of silver.

CHAPTER XVI.

THE SULPHATES.

SULPHURIC ACID ($H_2SO_4 = 98$) exists in the urine combined with organic and inorganic bases, but chiefly in the form of sulphates of potash and soda. The sulphates are present in only very small quantity in the fluids of the body with the exception of the urine. But the urine also contains sulphur in a state of incomplete oxidation, and this in the urine of patients suffering from certain diseases of the liver may form as much as 40 per cent. of the total sulphur present. This sulphur, oxidized with difficulty, is generally regarded as arising from biliary compounds in the urine, particularly derivatives of taurin, the amount varying under different circumstances, being generally large in constipation. To obtain this sulphur it is not sufficient to treat the urine with zinc and sulphuric acid and estimate the hydric sulphide evolved; only by the use of such powerful oxidizing reagents as nitric acid and potassic chlorate can the total amount be obtained (Lepine).

The Origin of the Sulphuric Acid.—It arises chiefly in the decomposition of albumen in the system, as the sulphates taken in the food are very slight in amount. It is difficult to say, however, how much is derived from tissue albumen and how much directly from food albumen.

When the albumen of the food falls in amount, so also does the sulphuric acid of the urine: in high fevers with much decomposition of organic albumen the sulphuric acid is likewise increased proportionally. The excretion of this acid would therefore appear to maintain a close relationship to the excretion of urea; but it must be remembered that while the nitrogen of albumen is more or less a constant quantity (16 to 17 per cent.) the sulphur varies considerably (1·25 to 1·6 per cent.); also a part of the sulphur is excreted by the intestine, while the whole of the nitrogen of the decomposed albumen passes away by the urine. Further, the whole of the sulphur is not in the form of sulphates in the urine; only 85 per cent. may be reckoned as such.

Amount.—Adult men excrete a mean of 2 to 2·5 grams sulphuric acid, of which the potash salt forms about 4·3 grams and the soda salt 3·55 grams, or 0·032 gram of sulphuric acid per kilo. in the 24 hours; for women the mean is about 1·96 gram. The quantity, however, varies even in the same individual from day to day, occasionally as much as 45 per cent. above or below the average mean.

The elimination is *increased* when the minerals of the food are augmented; an increase generally shows itself some hours after a meal, especially of animal food; also after prolonged exercise (Engelmann, denied by Voit), and after ingestion of soluble sulphates, sulphuric acid, or bodies containing sulphur, and also temporarily after copious draughts of water. It is *diminished* by vegetable diet, and less is excreted during the night and during pregnancy.

A pathological increase occurs after the ingestion of sulphur combinations, phenol, thymol, salicin, and liquor potassæ; also in delirium tremens and in other deliriums (Bence Jones), in acute inflammatory diseases of the nervous structures, and in acute inflammations generally, as pneumonia and acute rheumatism; in some cases of diabetes insipidus, and occasionally in some forms of skin disease. The sulphates are slightly increased in fevers, but diminished considerably during convalescence (Zülzer), though according to some authorities they are diminished in all acute and many chronic febrile attacks; indeed, it may be said that the sulphates are *diminished* to some degree in acute and chronic affections, probably on account of the lessened amount of food then absorbed. Likewise diminished in leukæmia, diabetes mellitus, eczema; also in inflammatory affections with much exudation, in chlorosis, and often in diseases of the nervous system.

Tests.—1. Add some drops of hydrochloric acid to the urine, and then *baric chloride:* a white precipitate of baric sulphate, insoluble in acids.

2. By acidifying the urine strongly with acetic acid, adding baric chloride, and then boiling, the preformed inorganic sulphates are thrown down; but the filtrate, when strongly acidified with hydrochloric acid and boiled, gives a further precipitate of sulphur, due to the organic sulphates. This separation may be better effected thus: Mix equal volumes of urine and baryta mixture [cold saturated solution of hydrate of baryta (2) and nitrate of baryta (1)]; filter, and having acidulated the filtrate with hydrochloric acid, boil, and the second precipitate is thrown down.

To avoid the difficulties encountered in the filtration of barium sulphate, silver nitrate should be added immediately after the precipitation of the sulphuric acid by the barium chloride; a flocculent precipitate is thereby obtained, which can readily be filtered. Removal of the silver chloride is effected afterwards by ammonia without any loss of the sulphate.

3. Sulphuric acid gives a precipitate with *chloride of lime* in moderately concentrated solutions, the resulting sulphate, however, being soluble in a large volume of water; also a white precipitate with *lead acetate*, soluble with difficulty in water and dilute acids.

Quantitative Estimation. I. *Gravimetric.* (*a*) *Of the Total Sulphuric Acid.*—Mix 100 c.c. clear filtered urine with 5 c.c. hydrochloric acid (sp. gr. 1·12), boil, and then add baric chloride to complete precipitation; continue to boil for some time until the supernatant liquid is clear, and throw it upon a small filter of Swedish paper that has been washed with dilute hydrochloric acid, collecting all the precipitate upon the filter with the help of a glass rod tipped with gum elastic. A little of the filtrate should early be tested with a drop of sulphuric acid, to ascertain the presence of excess of barium chloride. If this is the case wash the precipitate thoroughly with hot water, then with hot spirit, and afterwards with ether. Now dry the filter and its contents, and transfer them to a platinum capsule, where they are to be covered, heated to redness till quite white, allowed to cool, and then weighed. A slight loss occurs.

(*b*) *Estimation of the Sulphuric Acid Combined with Aromatic Organic Bases.*—100 c.c. urine and 100 c.c. baryta mixture (see under Urea) are mixed in a dry beaker, well shaken, and then thrown on a dry filter. Acidify 100 c.c. of the clear filtrate ($=50$ c.c. urine) strongly with hydrochloric acid, and boil for some time over a water bath until the precipitate is well settled down. Then proceed as above.

Calculation.—$233BaSO_4 = 98H_2SO_4 = 80SO_3 = 32S$. If we reckon as H_2SO_4, multiply the weight of $BaSO_4$ by $\frac{98}{233} = 0·4206$; if as SO_3, then multiply by $\frac{80}{233} = 0·3433$; and if as S, by $\frac{32}{233} = 0·1373$.

Example.—100 c.c. urine gave 0·490 $BaSO_4$, then the $H_2SO_4 = 0·490 \times 0·4206 = 0·206$ per cent., and the $S = 0·490 \times 0·1373 = 0·0672$ per cent.

II. *Volumetric.* (*a*) *Standard Baric Chloride.*—Some crystallized baric chloride is powdered, dried between folds of blotting-paper, and 30·5 grams taken and dissolved in distilled water, the solution being made up to a litre, 1 c.c. $= 0·01$ gram SO_3.

(*b*) A *dilute solution of sodic sulphate* is also prepared.

Process.—Measure 100 c.c. urine into a beaker, acidify with a little hydrochloric acid, and boil in a sand bath; let the baric chloride solution next flow gradually in so long as the precipitate distinctly increases. Then lay aside to allow the precipitate to subside; let a drop of the baric chloride now flow down the side of the beaker, and if a precipitate occurs continue to add the baric chloride until the whole of the sulphuric acid appears to be thrown down, and let it settle as before. Instead of waiting until the precipitate subsides, a little of the fluid may be filtered into a watch glass and tested with the baric solution, the whole being returned again to the beaker. This filtration may readily be effected by dipping into the beaker a wide open tube, over whose lower end a piece of filter paper has been tied, and removing it after a short interval. Care must be taken that an excess of baric chloride is not added. This is ascertained by testing a drop of the filtrate upon a piece of glass lying over a dark background with a sodic sulphate; if a precipitate is obtained then too much baric chloride has been added, and the titration must be repeated.

Suppose 18 c.c. have been added to obtain complete precipitation, then 0·18 gram SO_3 is present in the 100 c.c. urine.

CHAPTER XVII.

THE PHOSPHATES.

THE phosphoric acid of the urine is in part (two-thirds) in combination with alkalies, and in part (one-third) with the alkaline earths, lime and magnesia. Of these there are the acid phosphate of soda, $NaH_2PO_4 + H_2O$, to which LIEBIG ascribes in great part the acidity of the urine; the alkaline phosphate, Na_2HPO_4, possibly only in small proportion, for although this phosphate is generally met with in all the animal fluids it is the acid salt that is found principally in the urine. A potash phosphate is present in small amount. But the composition of the phosphates in the urine is liable to considerable variation: in acid urine the salts NaH_2PO_4 or $Ca(H_2PO_4)_2$ are generally present; when the urine is neutral, in addition to the above acid salts, we have Na_2HPO_4, $CaHPO_4$, $MgHPO_4$; while in alkaline urines the combinations Na_3PO_4, $Ca_3(PO_4)_2$, $Mg_3(PO_4)_2$ may also be present.

The *alkaline phosphates* are soluble in water, and are not precipitated from their solutions by ammonia or the alkalies, so that when ammonia is added to healthy urine the alkaline phosphates are not thrown down.

The *earthy phosphates* are insoluble in water, but readily soluble in such weak acids as carbonic and acetic; albuminous bodies and mucus have likewise some power in dissolving these phosphates. They are precipitated from their solutions by ammonia.

The ordinary *phosphate of soda* is soluble in water and alcohol; its aqueous solution has an alkaline reaction and absorbs carbonic anhydride very readily. When heated it melts, loses its water of crystallization, and ultimately changes into the pyrophosphate. The *acid phosphate*, on the other hand, is changed by heat into the metaphosphate, and is easily soluble in water, but insoluble in alcohol.

Uric acid has the power of decomposing the alkaline phosphates, a urate and an acid phosphate being formed.

The *ammoniaco-magnesian or triple phosphate* $(NH_4MgPO_4+6H_2O)$ is met with in the urine and in the animal fluids when these are undergoing alterations. The crystals are generally well marked, being most frequently found as vertical, rhomboidal, or triangular prisms with obliquely truncated ends; but if deposited rapidly from urine by the addition of ammonia, this phosphate may assume a stellate form, the crystals consisting of four or five feathery rays. Sometimes a thin pellicle is formed on the surface of urine, consisting of organic matter with numerous crystals of the triple phosphate.

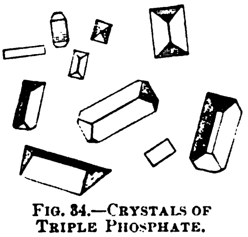


FIG. 84.—CRYSTALS OF TRIPLE PHOSPHATE.

Phosphate of lime is usually deposited in an amorphous condition, generally in minute transparent granules, but the deposit after a time may assume a crystalline form and appear as minute spherules or dumb-bells, or as fine needles grouped in globular masses. These crystals can be formed artifically by dissolving a little calcium chloride in a drop of glycerin, and a little phosphate of soda in another drop, and allowing the two drops to mix slowly under a cover glass: crystals will appear in a few days. Also by adding a little calcium chloride to normal urine, and nearly neutralizing it with caustic soda, crystals of the calcic phosphate may be obtained.

The urine from which one of these deposits occurs is generally alkaline. If uric acid, urates, and oxalate of lime are associated with the triple phosphate in a urinary sediment, they are thus distinguished:—

1. Warm the urine: the urates dissolve.
2. Add acetic acid: the phosphates dissolve.
3. Add caustic potash: uric acid dissolves.
4. Examine the deposit microscopically and apply the murexid test.
5. Dissolve in acetic acid and test with uranic nitrate for phosphoric acid, and with oxalate of ammonia in excess for lime; filter and add ammonia to the filtrate, and magnesia is precipitated as the phosphate.

Origin of Phosphoric Acid.—This acid is generally distributed in the tissues of the body; it is also contained in the food, and it is probable that the greater part of the phosphoric acid eliminated comes from the food ingested, partly as phosphates taken as such, and partly from phosphorus and phosphates previously combined with the proteids. About one-third to one-fourth, if not more, of these phosphates contained in the food, however, is excreted by the intestine. Another source of the phosphates is the decomposition of such bodies as nuclein and lecithin, which contain phosphorus: but the amount formed in nervous tissue is comparatively small.

ZÜLZER estimates the proportion of phosphoric acid to every 100 parts by weight of nitrogen in the tissues as follows: blood 4, muscle 15, brain and nervous system 45, while in the urine the proportion varies from 18 to 20.

Amount of Phosphoric Acid Excreted.—In the urine from 2·5 to 3·5 grams are excreted in the twenty-four hours, though it may rise to 5·5; the mean, however, may be taken as 2·8 grams, or 0·04 to 0·05 gram per kilo. of body weight, though it is given by VOGEL as high as 3·5 grams for well-fed healthy adults, or 0·064 gram per kilo. It forms about 3·22 per cent. of the urinary solids. Of the earthy phosphates the mean is 1·1 gram, the calcic salt = 0·4 and the magnesic = 0·6 gram.

The fæces also contain a variable proportion of phosphoric acid—a mean of 0·666 gram in the twenty-four hours, that is, one-fourth to one-fifth of the amount excreted in the urine (HAXTHAUSEN)—but the elimination by the fæces is increased by an abundant ingestion of carbonate of lime, the effect only, however, lasting a couple of days or so (RIESSELL).

Variations.—Great difference of opinion exists as to the effects of different physiological and pathological conditions of the body upon the elimination of phosphoric acid; it is very probable that the amount excreted is not constant, but subject to considerable variation.

(j) The *food* has an important influence, the phosphoric acid increasing for some hours after a meal, and diminishing during starvation or abstinence. The nature of the food has also an important effect, the phosphoric acid being more abundant after animal than vegetable food. A man upon a mixed diet eliminated in the urine the total phosphates contained in the food (BEALE).

An abundant ingestion of calcic carbonate increases the earthy phosphates: and the excretion of these phosphates may be said to run more or less parallel with the decomposition of albumen, an animal diet greatly increasing their amount and abstinence diminishing them. A mixed diet gives of earthy phosphates in a healthy man a mean of 0·944 to 1·012 gram (NEUBAUER), or 1·2 gram (BENCKE) in the twenty-four hours. The presence of much soluble phosphates or of phosphorus-holding bodies in the diet increases the elimination, as also much consumption of fluids. The food further greatly influences the proportion of the phosphoric acid to the nitrogen in the urine and fæces: with much animal diet the proportion is 1 : 8·1, while with bread diet it is 1 : 3·3. Indeed, it is very probable that the altered diet in diseased conditions accounts largely for much of the alteration in the amount of phosphates excreted.

(ii) *Active exercise* increases the phosphates (HAMMOND, ENGELMANN, PAVY, MOSLER), though this is denied (PETTENKOFER, VOIT, BYASSON).

(iii) *Cerebral activity* increases it, but there is much difference of opinion as to this. While MOSLER, BYASSON, etc., maintain that the elimination of the acid in the urine is increased by brain work, HODGES WOOD asserts that the total phosphoric acid remains constant, although the alkaline phosphate increases and the earthy phosphate diminishes.

(iv) *Time of Day.*—In the same individual the amount excreted exhibits considerable variation during the day. It increases after dinner, attaining its maximum in the evening, diminishes slightly during the night, and reaches its minimum in the morning (VOGEL). Its amount seems affected more or less by the same conditions as influence the amount of urea.

(v) Sleep appears to exercise little or no effect, but the amount is [illegible]

(vi) [illegible] after birth excrete about [illegible] compared with 0·19 to 0·23 [illegible] much less in growing [illegible] the quantity of earthy [illegible]

Reactions and Tests [illegible] gives a white [illegible] by hydrochloric and [illegible] phosphate must first [illegible]

[illegible] of the magne- [illegible] Now all this mix- [illegible] precipitate of [illegible] acid. If the [illegible] to appear.

[illegible] phosphate of [illegible] is present this salt will be precipitated first; the same also occurs with a chromate, so that if silver nitrate is added to a solution containing sodic chloride, potassic chromate, and a phosphate, the chloride is precipitated first, then the chromate, and lastly the phosphate.

4. *Molybdate of ammonia* dissolved in nitric acid gives with a phosphate a yellow, finely pulverulent precipitate, whose formation is favored by a gentle heat.

5. Acidify the urine with a few drops of acetic acid, and add *ferric chloride:* a thick yellowish white precipitate of ferric phosphate, which is easily soluble in the mineral acids, in the perchloride in excess, or in ammonia.' If any free acid is present in the urine add acetate of soda and free acetic acid before adding the ferric chloride.

6. Acidify as before and add some *uranic nitrate*, preferably to boiling urine; a dirty white precipitate of uranic phosphate is formed, that is easily soluble in the mineral acids.

7. The *earthy phosphates* in urine are precipitated by the addition of ammonia, stellate crystals being formed; filter and test the filtrate with ferric chloride after having acidified with acetic acid: a whitish yellow precipitate appears, indicating the presence of sodic phosphate. In the ammoniacal precipitate phosphate of lime and the triple phosphate are present. To separate the lime from the magnesia dissolve the precipitate in acetic acid, and add ammonium chloride and ammonium oxalate, when the lime will be thrown down; while the magnesia is separated from the filtrate in the form of triple phosphate by adding to it ammonia.

To separate all the phosphates contained in urine add to the latter a solution containing sulphate of magnesia (1), distilled water (8), ammonium chloride (1), and ammonia (44). They are deposited as the triple phosphate.

Quantitative Estimation. I. *Volumetrically by means of a Standard Uranic Solution.*—If to a solution of sodic phosphate (Na_2HPO_4) acidified with acetic acid a solution of nitrate or acetate of uranium is added, we obtain a yellowish white precipitate, the whole of the phosphoric acid being thrown down as uranic phosphate:

$$4(UrO.NO_3)+2Na_2HPO_4 = 2(Ur_2O_3)P_2O_5+4NaNO_3+H_2O.$$

This precipitate has a molecular weight of 368[$Ur = 120$, $H = 1$, $2(UrO) = 272$, $PO_4 = 95$], corresponding to 71 P_2O_5 or 98 H_3PO_4.

Any excess of uranic salt is easily detected by testing a drop of the mixture with a drop of potassic ferrocyanide on a white porcelain plate, which gives a reddish brown precipitate with any uranic salt not combined with phosphoric acid. This body is therefore used as the indicator of the terminal reaction.

To effect the analysis a solution of known strength of the uranic salt is made, which for accuracy is titrated with a standard solution of sodic phosphate; and to insure the free acid of the urine being acetic, in which the precipitate is insoluble, this fluid is first treated with a solution of acetate of soda containing free acetic acid. But in presence of sodic acetate it should be noted that the reaction of the ferrocyanide with excess of uranic salt is not so sharp as with the pure salt, the production of the chocolate color also being retarded.

Preparation of the Solutions.—(*a*) The *ferrocyanide solution* consists of 1 of the salt in 20 of water freshly dissolved.

(*b*) *The Acetate of Soda Solution.*—Dissolve crystallized sodic acetate 100 grams in water, add strong acetic acid 100 c.c., and make up to 1,000 c.c. with water.

(*c*) *The Sodic Phosphate Solution.*—Roughly powder some pure crystals of the phosphate ($Na_2HPO_4+12H_2O$), and dry them between sheets of filter paper. Now weigh 10·085 grams and dissolve in 1 litre water. This solution will contain 0·2 P_2O_5 in 100 c.c.

(*d*) *The Uranic Solution.*—This is best prepared so that 20 c.c. correspond to 50 c.c. of the sodic phosphate solution, and therefore to 0·1 gram P_2O_5. Accordingly the litre should contain 20·3 grams pure uranic oxide.

Dissolve 33 grams yellow uranic oxide in nitric acid (sp. gr. 1·2), or in dilute acetic acid, and dilute up to 1,100 c.c. (An approximative solution may also be obtained by dissolving 40 grams of the uranic acetate or nitrate in a litre of water to which 25 c.c. pure glacial acetic acid have been added.)

Fill a burette with this solution; measure 50 c.c. of the standard phosphate into a small beaker, and add to it 5 c.c. sodic acetate solution; some drops of the ferrocyanide are next to be placed upon a white porcelain plate.

Now boil the phosphate solution in the small beaker, and allow about 18 c.c. uranic solution to flow into it; boil again, and having stirred well, bring a drop of the mixture in contact with one of the drops of ferrocyanide (or bring a drop of the ferrocyanide into the centre of a drop of the mixture placed on the porcelain plate): if a faint brown color appears in a few seconds then an excess of the uranic salt has been added, but if no brown color shows itself then more of the uranic solution is to be dropped in; this addition must be made very gradually, and the mixture tested with the ferrocyanide after each addition. As soon as ever the reddish brown color appears boil the whole mixture again with frequent stirring, and repeat the ferrocyanide test. A second, and even a third, experiment should be made with the first as a guide, and great care taken with the final addition of the uranic solution, so as to have the least possible excess.

Suppose instead of 20 c.c. only 19·2 c.c. were required, then the solution must be diluted in this proportion: $\frac{20}{19{\cdot}2} = 1{\cdot}04166$ litre, or to 1,000 c.c. of the uranic solution 41·66 water added. It is better, however, to add less water than this at first, and to titrate again. 20 c.c. of the solution thus prepared = 0·1 P_2O_5.

Titration of the Urine. (A Mohr's burette, a piece of white porcelain, and two pipettes, one for delivering 50 c.c. and the other 5 c.c., are required.)

(j) *To Obtain the Total Phosphoric Acid.*—Heat to boiling 50 c.c. of the filtered urine to which 5 c.c. of the sodic acetate solution have been added; then titrate with the uranic solution as above, boiling and stirring well after each addition and testing a drop from time to time with the ferrocyanide; continue to add the uranic solution so long as a precipitate is seen to occur, and till the brownish yellow color is obtained as above with the ferrocyanide. Two determinations must be made.

If 22·5 c.c. uranic solution were required for the appearance of the terminal reaction, then (20:22·5 = 0·1:0·1125) 50 c.c. urine contain 0·1125 gram P_2O_5, or 2·25 grams in the litre.

It may be interesting and advantageous to know the amount of the phosphoric acid combined with lime and magnesia; this is done as follows:—

(ij) *To Estimate the Phosphoric Acid Combined with the Alkaline Earths.*—Take 200 c.c. filtered urine, render it freely alkaline with ammonia, and lay aside for 12 hours. Collect the precipitated earthy phosphates on a filter, where they are to be washed with ammoniacal water (1 to 3); and after having made a hole in the filter wash the precipitate through with water containing a few drops of acetic acid into a small beaker, in which they are to be dissolved in as little acetic acid as possible with the aid of heat. Now add 5 c.c. of the sodic acetate solution, bring the volume up to 50 c.c., and titrate as before.

If, for example, 10·5 c.c. of uranic solution have been required, then, as 10 c.c. of this solution = 0·05 P_2O_5, 10·5 c.c. = 0·0525 gram P_2O_5 in every 200 c.c. of the urine, or 0·2625 P_2O_5 in the litre.

(iij) *To Obtain the Phosphoric Acid Combined with the Alkalies.*—Subtract the phosphoric acid of the earthy phosphates from the total phosphoric acid obtained, and the difference will be equal to the acid combined with alkalies. Thus—

Total phosphoric acid	2·25
Phosphoric acid combined with the alkaline earths.	0·2625
" " " alkalies . . .	1·9875

II. *Quantitatively by Precipitation with Molybdate of Ammonia.*—Teissier has employed a solution of molybdate of ammonia, made by dissolving 100 grams in 100 c.c. ammonia and adding the solution slowly to 1,000 c.c. nitric acid.

5 c.c urine are evaporated and the residue dissolved in 5 c.c. pure nitric acid; to this 5 c.c. water are added and the solution filtered. Pour this into 5 c.c. of the molybdate solution contained in a capsule. The precipitate having been allowed to settle, is collected, washed, dried, and weighed. The weight × 1·63 gives the phosphorus in 1 litre, or × 3·735 gives the phosphoric acid. The process is difficult but exact.

III. Teissier has also proposed the following method for the *approximative determination of the phosphoric acid by the volume of the triple phosphate precipitate obtained.* It gives very fair results and is easy of application:—

If the urine is not acid add a few drops of nitric acid, in order to dissolve up any precipitated phosphates. Into a graduated cylinder pour 50 c.c. of the urine, and saturate it with a solution containing sulphate of magnesia (1), ammonium chloride (1), ammonia (1), and distilled water (4). Shake well and lay aside for 24 hours. All the phosphoric acid is precipitated as triple phosphate. The precipitate settles, and its height is to be read off in the graduated cylinder. 1 c.c. of the precipitate corresponds pretty closely to 0·30 gram phosphoric acid per litre, representing about 0·60 to 0·70 gram of phosphate. Knowing the quantity of urine passed in the 24 hours, we can thus readily obtain the daily total excretion of phosphoric acid.

IV. *Estimation of Lime and Magnesia Phosphates.*—Precipitate 100 c.c. urine with ammonia, dissolve the precipitate in acetic acid, and add sufficient oxalate of ammonia to throw down all the lime; let the precipitate settle, then decant and collect it on a filter, where it is to be washed with hot water. The filtrate and washings are to be laid aside and subsequently tested for magnesia. The precipitate is to be well washed with water, acidified with sulphuric acid, diluted freely, and titrated with a decinormal solution of potassic permanganate (3·16 grams to the litre), the latter being added from a burette until it ceases to lose its color. Each c.c. of the permanganate represents 0·0028 gram CaO.

To the filtrate and washings ammonia is added, and then sodic phosphate; lay aside for 10 hours or so in a moderately warm place; the precipitated ammonio-magnesian phosphate is collected on a small filter, washed in ammoniacal water, then dissolved in acetic acid, and titrated with uranic solution as in I. Each c.c. of this solution represents 0·0028 gram magnesia.

Pathological Alterations.—The phosphates excreted are diminished slightly in acute diseases, the result most probably of deficiency in the diet; but in most fevers, nevertheless, there is an increased proportion of phosphates. As a general rule the alkaline phosphates increase and diminish at the same time as the sulphates, and accordingly seem to have their origin in the retrograde metamorphosis of the proteids. The diminution in the alkaline phosphates coincides with the acute periods of febrile affections; while they reappear more abundantly when the disease returns to its natural course and tends toward a cure. In pneumonia, for example, when the fever diminishes the alkaline phosphates increase, and thus indicate the beginning of convalescence.

An *increase in the total phosphates* is observed in acute inflammatory diseases of the nerve structures, temporarily in acute febrile diseases, though diminished in the course of the disease (VOGEL, TEISSIER), occasionally in paroxysms of acute mania, and in brain tumors; increased also in the acme of chorea, in acute atrophy of the liver (BOUCHARD), in diabetes (LECORCHÉ), in the early stages of phthisis, and in chronic rheumatism, leukæmia, and osteomalacia.

A *decrease* may be noticed in the stage of exhaustion in mania, in acute dementia (SUTHERLAND and BEALE), and generally also in chronic affections of the brain (MENDEL). During paroxysms of acute mania, and also in epilepsy, general paralysis, melancholia, and dementia, the quantity of the urine, and the amount of the sodic chloride, urea, and phosphoric and sulphuric acids have been noticed to be less during convalescence (ADAMSON); while in chronic melancholia the chlorides, urea, and phosphoric and sulphuric acids are much reduced. A diminution in the discharge of phosphates is also often to be seen in certain forms of Bright's disease and cardiac affections; in diseases of the digestive organs hindering absorption (BRATTLER); in chlorosis and during the pyrexia of intermittent fever; and in rickets, gout, arthritis, and chronic rheumatism.

So far as *drugs* are concerned its amount is increased by lactic acid and carbonate of soda, but diminished by morphia, chloral, chloroform (though occasionally increased by this body), ether, and alcohol.

The *earthy phosphates* do not appear to be much affected by different diseases, although they are often *increased* in the urine of rheumatic patients; but if pericarditis sets in then the phosphates are immediately diminished (HELLER), but reappear in excess when this complication tends to disappear; also increased in osteomalacia, rickets, periostitis, and acute cerebral inflammations.

As a general rule they are *diminished* in typhus, chronic renal affections, organic diseases of the heart, in certain neuroses and spinal affections, and in some disturbed conditions of the alimentary canal.

Urinary sediments of the earthy phosphates, particularly of lime, are observed in rickets, osteomalacia, osseous caries, meningitis, and many other neuroses; at the same time there is generally also a diminution in the acidity. These deposits are frequent in cases of dyspepsia and over-work, but they are not necessarily indicative of increased nerve waste.

In chronic affections of the bladder the result of calculi, paraplegia, etc., deposits of crystals of the triple phosphate are frequent, the ammonia acting on the magnesic phosphate frequent in the urine, and the triple phosphate separating on account of its insolubility in an alkaline liquid.

The earthy phosphates are held in solution in normal urine, owing to its normal acidity and to its chlorides and carbonic acid. They are precipitated when the carbonic acid escapes on boiling, or on exposure to the air, or when an ammoniacal fermentation is set up and ammonic carbonate formed.

A deposit does not necessarily indicate an excess. The deposit that often occurs when urine is heated may be due to earthy phosphates and not to albumen. The sediment that so frequently forms in an alkaline urine and in certain chronic diseases generally contains 67 per cent. magnesia and 33 per cent. calcic phosphate (NEUBAUER).

Teissier has described, under the name of *phosphatic diabetes*, a morbid condition in which there is polyuria accompanied by increased elimination of phosphates—as much even as 12 to 20 grams in the 24 hours.

CHAPTER XVIII.

THE SALTS OF THE ALKALIES.

To *detect the soda and potash* in the dry residue of urine the ordinary method can be adopted of placing a little of this on a platinum wire in a Bunsen's flame; the soda imparts a brilliant yellow color, and if the flame is examined through a piece of cobalt glass it will be seen to be violet-tinted.

To estimate the soda and potash mix 50 c.c. urinė with an equal volume of baryta mixture, and after it has stood some time filter. Evaporate 80 c.c. of the filtrate ($= 40$ c.c. urine) to dryness in a platinum or porcelain dish, ignite, dissolve the cold residue in a little hot water, add ammonic carbonate to complete precipitation, filter, and wash the precipitate; the filtrate acidified with hydrochloric acid is then evaporated to dryness, and the residue gently heated to expel ammoniacal salts. This last residue is then treated with a few drops of ammonia and ammonium carbonate, its solution filtered, the filter washed, and the filtrate and washings evaporated to dryness in a platinum capsule of known weight; the whole to be again weighed after having been ignited and allowed to cool. This gives the total sodic and potassic chlorides.

The *quantity of combined ammonia* excreted in the 24 hours averages 0·724 gram. It is increased by the use of asparagus, and pathologically we meet with an increase in gout and diabetes; a considerable diminution in acute rheumatism, albuminuria, and phthisis; and a still greater diminution in erysipelas, small-pox, and typhus.

Estimation of Ammonia.—1. To a measured quantity of urine add some milk of lime and place under an air-tight bell jar in which there is also present a measured amount of acid of known strength. After 24 to 36 hours the acid is to be titrated with the standard alkali (see under Acidity of Urine) to ascertain the loss of acidity corresponding to the ammonia absorbed (Schlösing).

2. The following method is applicable where the urine has not undergone decomposition: Exactly neutralize 100 c.c. urine with normal alkali until a piece of violet litmus paper streaked with a fine glass rod that has been immersed in the fluid shows no change of color. Then transfer the whole to a large flask, and after the addition of 10 c.c. normal alkali boil until no more ammonia can be detected in the escaping vapors. When the flask has slightly cooled its contents are transferred to a tall beaker, and there titrated with normal nitric acid until violet-colored litmus is not stained when streaked as above with

a little of the solution. The number of c.c. of normal acid are deducted from the 10 c.c.of alkali, and the rest estimated as ammonia. 1 c.c. normal alkali = 0·017 gram ammonia.

The normal nitric acid (63 grams nitric acid per litre) is prepared of such a strength that 20 c.c. of it are neutralized by 1 gram of pure Iceland spar in small pieces, or of pure sodic carbonate that has been ignited.

CHAPTER XIX.

ABNORMAL CONSTITUENTS.

THESE may be different forms of albumen, blood, grape sugar, biliary acids and pigments, mucin, leucin, tyrosin, cystin, cholesterin, and fat; these bodies will be referred to in detail. In addition several other bodies may be met with, such as milk sugar, inosit, dextrin, peptone, melanin, allantoin, lecithin, acetone, alcohol, hydric sulphide, etc.

ALBUMINOUS URINE.

No other pathological constituent possesses the same interest for the physician as albumen; but even in healthy urine small quantities of albumen may be present. LEUBE believes that it may be detected in 4 per cent. of normal urines in a proportion not exceeding 0·1 per cent. In some of these, however, it may only appear after severe bodily exertion.

Serum albumen and serum globulin are the forms most frequently present, particularly the serum albumen; the serum globulin shows itself most frequently in acute inflammatory affections of the kidney and in amyloid disease of the same organ, and often also in catarrh of the bladder, but very little is present in most chronic inflammations of of the kidney (SENATOR). In albuminous urine we may also meet, and indeed according to SENATOR, nearly always, with albuminoid bodies such as peptone and the like; but according to GERHARDT this only occurs in cases of profound tissue alteration of the organism, as occasionally in diphtheria, typhus fever, and phosphorus poisoning. Peptones have also been met with in the urine in cases of acute nephritis (PETRI, EICHWALD), as also in acute yellow atrophy, and phosphorus poisoning.

Under a certain degree of pressure albumen will pass through an animal membrane. Thus, in experiments of GOTTWALT'S when albuminous fluids were allowed to rest upon or to flow under different pressures over the membrane, the filtrate was found to increase with the pressure, but in no definite ratio: the amount of albumen in the filtrate was always less than in the original fluid: e.g. egg albumen solution gave 72 per cent.; fluid from an ovarian cyst, 70 per cent.: blood serum, 60 per cent.: hydrocele fluid, 40 per cent. The percentage of globulin was still less, serum albumen and serum globulin passing through the membrane in the ratio of 3 to 2.

Characters.—Albuminous urine is pale or greenish yellow in color, of a low specific gravity (1006 to 1014), and not generally clear soon after being passed; usually also after standing a short time it deposits more or less sediment, which may consist of casts, clots, epithelial or pus cells; a froth forms readily on shaking.

Amount.—In moderate cases 6 to 8 or 4 to 10 grams of albumen in the twenty-fours is the average; in severe cases, 10 to 12 grams, or even as high as 30 grams. The average amount present in acute cases of albuminuria is $\frac{1}{10}$ to $\frac{1}{2}$ per cent., seldom over 1 per cent., though it may rise to 4 per cent.

A loss of 2 grams in the twenty-four hours has little influence on the blood and nutrition, while a loss of 6 to 8 grams may be regarded as moderate, but as considerable when it exceeds 10 to 12 grams (VOGEL). A constant daily loss of albumen must ultimately reduce the proportion of albumen in the blood, and produce a condition of hydræmia favorable to the occurrence of dropsies; but so long as the digestion and appetite keep good the constitution of the blood remains long comparatively unimpaired.

Tests.—The student should carefully perform for himself the experiments detailed in pp. 103, 104, and note the readiness with which albumen is changed into an albuminate when only a small amount of albumen is present and a very slight excess of acid or alkali. In testing for albumen in urine he should therefore guard against this source of error by *never adding less than $\frac{1}{10}$ the volume of the urine of nitric acid.* Further, the urine should be perfectly clear: this can generally be effected by filtration, but occasionally this is not sufficient; some calcined magnesia should then be added and the whole well shaken; or a few drops of a solution of sulphate of magnesia and then of sodic carbonate, and the mixture shaken as before. The filtrate will now pass through clear.

1. *The Test by Boiling.*—Normal urine of acid reaction generally remains clear on boiling, or if a flocculent precipitate occurs it is due to earthy phosphates—a separation more likely to occur with a neutral or alkaline urine. Always, therefore, before applying this test, ascertain the reaction of the urine, and if it is alkaline, first acidify with a little acetic or nitric acid; and to avoid a solution occurring of the albumen, which would be possible *if only a trace were present*, it is best to proceed thus: Acidify with very little acetic acid, then add $\frac{1}{6}$ the volume of the urine of concentrated solution of sodic chloride, magnesic sulphate, or sodic sulphate; on boiling any albumen present will be precipitated. The separation of the albumen generally occurs about 50° to 60°, in acid urines containing sodic chloride generally from 70° to 72°, the coagulation first showing itself at the surface; but when only a trace of albumen is present separation may not occur till boiling point is reached.

It should be remembered that when a large amount of mucin is present in urine the addition of acetic acid may cause a precipitation of this body, and thus lead to the presence of a trace of albumen being suspected. Accordingly, if much mucin is present, filter before boiling.

The test may be conveniently applied in this way: Fill a long test tube ¾ full with urine, then holding the tube by its lower end heat the upper third or so of the urine. Even a slight opalescence is thus rendered perceptible. A few drops of nitric acid are then added.

When the urine is turbid, but clears up as the temperature rises, an excess of urates is present. In some cases of osteomalacia a proteid body is present in urine, which is precipitated by boiling, but disappears on the addition of nitric acid, reappearing again, however, as a yellowish jelly when the liquid cools.

2. *The Nitric Acid Test.*—Treat a little of the urine with one-third its volume of pure nitric acid (sp. gr. 1·2): if the urine remains clear there is no albumen, or only a trace. Heating is unnecessary, but it is generally advisable first to boil the urine and then to add nitric acid in excess, when any precipitate due to earthy phosphates will disappear. Occasionally prolonged boiling after the addition of the acid gives rise to a slight muddiness even in urine free from albumen, but to what this is due it is difficult to say.

A separation of urates may also occur, which is liable to be mistaken for albumen; but the urates disappear, while the albumen remains when the urine is heated. Excess of uric acid may also cause a precipitate, but it does not generally form immediately, and the crystalline character of the deposit is characteristic. This excess of uric acid has been met with in typhoid fever and certain liver affections. If only traces of albumen are present, prolonged boiling after the acid has been added may dissolve the albumen, forming an acid albuminate that is not precipitated by heat. The use of certain resins, essences, turpentine, copaiba, cubebs, etc., may cause an opalescence when the acid is added, but alcohol causes this to disappear, and it also disappears when the urine is heated; there is in addition a characteristic smell evolved.

This test may be applied with great delicacy by HELLER'S *method:* Pour into a wide test glass some pure nitric acid until it forms a layer about half an inch deep; then by means of a pipette allow the urine, which should be clear, to flow slowly over the surface of the acid. If albumen is present *a ring of opalescence, sharply limited above and below, appears at the line of contact of the two liquids.* The acid may also be allowed to trickle slowly down the side of the inclined test glass containing the urine, so as to accumulate below that fluid. A little time should always be allowed to elapse before pronouncing upon the absence of the hazy cloud indicative of albumen; and this caution is particularly necessary when only a trace of albumen is present. The opalescence is best seen by standing before a window and holding the tube on a level with the eye in front, say, of the sleeve of a dark coat, with the light falling obliquely upon the test glass from above. (*a*) A ring showing itself at a higher level, and not so sharply defined superiorly, is due to excess of urates. Sometimes two rings may make their appearance, one at the line of contact of the urine and the acid, due to albumen, and the other higher up, due to excess of urates. If there should be any difficulty as to the identity of the urates, insert the test glass in boiling water, and the cloud of urates will gradually disappear as the urine becomes heated; further, the addition of acetic acid to a fresh specimen of the urine causes a similiar precipitate, but no coagulation of albumen. In the case of a turbid urine, generally the result of the presence of excess of urates, the turbidity should first be removed by gently heating the urine. (*b*) Very concentrated urines may give a crystalline precipitate of nitrate of urea at the line of contact, but, besides being crystalline in appearance, it disappears when the urine is diluted or gently heated; it is also slow in forming. But, to avoid any mistake from urea or urates, dilute the urine with two or three times its volume of water before testing it.

Often at the line of contact of the two fluids a violet or blue coloration may show itself, due to indican.

3. *Acetic or Citric Acid and Ferrocyanide Test.*—Acidify strongly with acetic or citric acid, and add some drops of potassic ferrocyanide solution: a white flocculent precipitate appears; even very dilute solutions give a turbidity.

4. *The Picric Acid Test.*—This is also strongly recommended by some authorities, a saturated watery solution being used, and it is best applied after HELLER'S method with nitric acid, a narrow greenish zone or cloud appearing at the junction of the two fluids. It forms in a minute or so, even if the albumen is present in only very small quantity. It is not so applicable where there is turbidity from urates or phosphates (KIRK). According to Dr. G. JOHNSON "there is no known substance occurring in either normal or abnormal urine, except albumen, which gives a precipitate with picric acid insoluble by the subsequent application of heat." The presence of quinine in the urine, which always occurs when this alkaloid is administered, causes an opalescence when the picric acid test is employed; but all turbidity is dissipated by heat. But this reagent, it should be remembered, also precipitates albumose and peptones.

In addition to the above, reference will be made here to a few other tests that are regarded as delicate.

5. *Phosphotungstic acid* gives a precipitate even with very dilute solutions of albumen. Potassio-mercuric iodide or mercuric chloride with citric acid are also good precipitants. (See p. 104.)

6. A solution of *taurocholic acid* precipitates albumen, but not peptone.

7. *Metaphosphoric acid* exceeds all other known reagents in the completeness of its precipitation of albumen (HINDENLANG).

8. Add a little crystalline trichloracetic acid to 1 c.c. clear filtered urine, and leave the mixture at rest. The acid dissolves, and at the juncture of the two layers of liquid a well-defined cloudy ring forms. When much urates are present, warm, and the turbidity caused by them disappears, but not that formed by albumen.

9. When the urine is suspected to contain peptones the last traces of albumen are removed by lead acetate, then treated with one-fifth its volume of acetic acid, and finally with a solution of sodic phosphotungstate acidified with acetic acid: any cloudiness or precipitation indicates peptone. Even very dilute solutions of peptones yield a distinct opalescence with picric acid. Peptones also gives a pinkish coloration with *Fehling's solution*, this reagent giving a bluish tint with albumen

(p. 120). Pour a little of the urine upon some *Fehling's* solution contained in a test glass, and at the junction of the two fluids a phosphatic cloud will show itself, above which there will be seen a rosy-tinted layer if there are peptones only in the urine, but with somewhat of a violet coloration when albumen is likewise present. On adding some picric acid the color becomes reddish, and finally yellow.

To Separate the Albumens from Urine—1. A series of methods are given on p. 102.

2. Occasionally forms of albumen may be present in urine which give no precipitate on boiling or after the addition of nitric acid, but in which a precipitate is obtained by alcohol. In a few cases the urine has assumed an opalescence on dilution, owing to the presence of paralbumen and paraglobulin, which was increased by a current of carbonic acid gas (SENATOR). To detect or separate the paraglobulin dilute the urine to sp. gr. 1002 with water, and pass a current of carbonic acid gas for three or four hours; let the whole stand for a day or so, and a whitish precipitate is deposited.

Or the globulin can also be separated by saturating the albuminous urine with magnesic sulphate; the filtrate contains the serum albumen. The precipitate is washed with hot water until the filtrate is free from sulphuric acid and the globulin not only washed but coagulated; it is then to be dried and weighed.

Occasionally only paraglobulin is present in pathological urine, but we frequently find the albumen in this fluid consisting of paraglobulin two-thirds and serum albumen one-third.

It is rather difficult to *separate serum albumen and peptone* when they are in the same urine, but the process can generally be effected as follows; Strongly acidify the filtered urine with acetic acid and lay aside for 12 hours; decant and filter the supernatant liquid; then add an excess of a strong solution of ferric chloride, and afterwards neutralize with sodic carbonate. Decant and filter again after some time, evaporate the filtrate to a small bulk, and add excess of absolute alcohol; the peptones are thrown down as a brownish precipitate. By boiling this with alcohol, washing it with ether, dissolving it in water, then reprecipitating with alcohol, and repeating the drying and washing of the precipitate with ether, a yellowish powder is obtained (SCHULTZEN, etc.).

Quantitative Estimation. 1. *After* SCHERER'S *Method.*—100 cc. of the clear urine are placed in a beaker of about 200 c.c. capacity, and if the reaction is not markedly acid a drop or two of acetic acid is added. It is then heated for half an hour or so in a water bath until the precipitate settles, which is sometimes expedited by the cautious addition of a trace of dilute acetic acid. Pour upon a small Swedish filter that has been dried at 110° and weighed, aiding the filtration by a gentle exhaustion, and collect the albumen on the filter, where it is to be washed with boiling water rendered ammoniacal to remove uric acid and urates, and then with hot water alone till the filtrate gives no reaction of chloride; it is next to be washed with absolute alcohol and subsequently with ether, afterwards dried at 110° and weighed.

The operation requires four to five hours, but without much care the results are inaccurate, and, as it is difficult to precipitate the albumen completely, they are also too low.

If the urine is very rich in albumen it is better to take only 20 to 50 c.c. and dilute up to 100 c.c. before boiling. If much mucus is present it is advisable to dilute the urine with twice its volume of water and add acetic acid (15 drops to every 100 c.c.); filter after 24 hours; the filtrate is then boiled for some time, either alone or after the addition to the urine of $\frac{1}{10}$ its volume of nitric acid.

2. *By the Polariscope.*—When the urine is absolutely clear and free from sugar, and the amount of albumen considerable, the estimation may be made by means of the polariscope. The clearing up can usually be effected by treating the urine with acetic acid, sodic carbonate, or milk of lime, or with magnesic sulphate and carbonate of soda.

Proceed as in the examination of sugar, using VENTZKE-SOLEIL'S instrument, and arranging by means of the compensator so that the two halves of the field of vision are equally colored at the *teinte de passage* (generally the zero of the instrument); the two-decimetre tube is to be filled with the clear filtered urine, and the compensator then turned till the two halves of the double plate are again colored alike, or till the same *teinte de passage* is obtained as existed before the urine was inserted between the prisms. The zero of the vernier is now on the left side of the zero of the scale. Read off the number of divisions; each division corresponds to one gram albumen for 100 c.c. urine, and each division of the vernier representing $\frac{1}{10}$ gram.

If a decimetre tube is used instead, then multiply by 2 the degrees of the scale and vernier. More correctly the percentage will be found by the formula—

$p = 56\frac{a}{sl}$ $p =$ the weight of substance in 100 c.c. urine.
$s =$ the specific rotary power.
$l =$ the length of tube.
$a =$ indication of the scale.

3. ESBACH'S *Method of Deposits.*—The reagent employed is *prepared* by mixing 950 c.c. of a solution of picric acid containing 10 grams in the litre with 50 c.c. acetic acid (specific gravity 1·067) shake well and lay aside. Specially prepared tubes of glass about 6 inches high, 0·6 inch wide, and graduated in grammes, are required. There are two marks engraved on each tube, and up to the level of the lower mark it is to be filled with the urine, and up to the higher mark with the reagent.

Process.—If the urine has a higher specific gravity than 1006 to 1008, dilute it, noting the amount of water required, and if it is not acid add a few drops of acetic acid and stir well. Then fill the graduated tube with the urine and the reagent as just described; close the tube with the finger and turn it upside down several times, so as to mix the two fluids. The tube is next to be laid aside for 12 hours and the level of the deposit of albumen read off, which will give the number of grams of albumen present. If the urine has been diluted on account of its density, of course this must be taken into consideration.

For clinical purposes the indications are sufficiently exact, as I have found by comparison with SCHERER'S gravimetric method. It is also very easy of application.

4. *Rough Clinical Method of Deposits.*—As a means of comparison as to the relative amount of albumen discharged from day to day, the ready method is frequently adopted of boiling daily in the same sized test tube the same amount of urine passed about the same hour of the day, and then adding 3 or 4 drops of acetic acid; the tube is laid aside, and the height of the deposit as compared with the volume of the urine noted; or, if no deposit, the degree of opalescence or cloudiness. Only by using urine secreted as nearly as possible under similar conditions as to time, etc., testing equal amounts, boiling for a definite time, and noting the height of the deposit after a certain period has elapsed, can any even widely approximative results be obtained.

5. ROBERTS'S *Dilution Method.*—When an albuminous urine is progressively diluted with water and tested at frequent intervals with nitric acid after HELLER'S method, it will be noticed that the resulting precipitate or opacity becomes less and less, until at last it vanishes; when this happens less than 0·0014 per cent. albumen is present. With the increasing dilution the opacity also takes

a longer time in appearing. Acting on this Dr. ROBERTS dilutes the urine until it *gives no opalescence for* 30 *seconds after the addition of the acid, but shows it at the 45th second.*

The urine is first tested in the ordinary way, so as to form an estimate of the albumen present. It is then diluted 10 to 100 times, as deemed necessary, and a test tube about ¾ inch wide is filled to the depth of an inch or so with the diluted fluid. With a pipette a definite quantity of nitric acid (about 10 to 12 minims) is next allowed to flow into the obliquely inclined test tube, so as to form a layer below the urine a quarter of an inch deep. The time of the addition of the acid should be exactly noted, and also the time in which the opacity appears, which may be more readily seen by holding up the test tube to the light against some dark background. The experiment should be repeated with more or less diluted urine until the reaction appears in not sooner than 35 and not later than 45 seconds after the addition of the acid. The degree of dilution is then noted. If, say, to arrive at this result, 5 c.c. have been diluted up to 500 c.c. the urine is considered as having 100 degrees of albumen, each degree corresponding to 0·0034 per cent. [0·008 (MUSCULUS), 0·0033 (HAMMARSTEN)]; and each volume of water required to be added being termed a degree, the zero being the state of dilution necessary for the terminal reaction.

6. BÖDEKER's *Method: Precipitation with a Standard Solution of Acetic Acid and Potassic Ferrocyanide.*—This gives fairly approximative results when the albumen is not less than 1 to 2 per cent. The precipitation occurs in the proportion of 211 of the ferrocyanide to 1.612 albumen. Dissolve 1·309 gram pure ferrocyanide in 1 litre distilled water: 1 c.c. = 0·01 gram albumen.

Process.—Mix 50 c.c. of the albuminous urine with 50 c.c. ordinary acetic acid, and transfer the mixture to a burette. Five or six small filters are placed in as many funnels, and after having been moistened with a little acetic acid are filled with boiling water. Now measure 10 c.c. ferrocyanide solution into a beaker, and add to it 10 c.c. of the mixture of urine and acetic acid: shake well and filter: test the filtrate, if bright clear and yellow, with a drop of urine and note if any cloudiness is produced. If the filtrate is turbid, and gives an increased turbidity on the addition of the ferrocyanide, then the albumen has not been all precipitated. The experiment is then to be repeated with more or less of the ferrocyanide, according to the result of the first experiment: and this is continued until a nearly exact result is obtained.

7. TANRET's *method* is founded on the precipitation of albumen by potassio-mercuric iodide in presence of acetic acid. It is thus prepared:—

	Grams.
Potassic iodide	3·32
Mercuric chloride	1·35
Water	64·0
Acetic acid	20 c.c.

1 c.c. of this precipitates $\frac{1}{25}$ of a gram of albumen. It is to be added carefully and slowly till all precipitation is completed, which can be determined by allowing the precipitate to settle and adding a drop of the reagent to the supernatant liquid or to a few drops of the filtrate.

CHAPTER XX.

PATHOLOGY OF ALBUMINURIA.

THE cases in which albuminuria appears are very numerous.

1. *Renal Affections.*—In a great number of the cases of albuminuria the kidneys have undergone *structural alteration.* LANGHANS and

ave detected changes in the epithelium of the Malpighian capons of the epithelial lining of the tubes also frequently occur, ion of this epithelium as well as casts in the tubes may be any consequent albuminuria (SCHACHOWA). It is proboid degeneration of the kidney not involving the capsules or a long time without any albumen in the urine (LITTEN). ria may therefore be the direct consequence of renal disease, *cute inflammation* or *congestion* and in the *different forms of ht's disease of the kidneys.* As a *temporary phenomenon* it may noted in the congestion often resulting upon paralysis of the vasomotor nerves of the kidneys, and occasionally recurring in *specific and inflammatory fevers*, attended with a high temperature, as in scarlatina in an early stage, and during convalescence in typhus, typhoid, variola, erysipelas, and diphtheria; and in meningitis, pneumonia, peritonitis, acute rheumatism, especially when accompanied by pericarditis, pneumonia, or pleurisy; and in puerperal fever, particularly when attended with puerperal convulsions. If the temperature should continue high for some time (above 104° F.) peptones may also be present. In some individuals there is a great tendency to this occurrence of albuminuria in the course of different febrile attacks; but albuminuria is a recognized sequela of scarlatina, and a frequent occurrence in variola, typhoid, erpsipelas, malignant pustule, and diphtheria. The congestion of the kidneys leading to the presence of albumen in the urine may also result from the irritation of powerful diuretics, cantharides, carbolic acid, etc.

Retention of the urine through closure of the ureters may likewise lead to albuminuria, the epithelium lining the tubules becoming granular and fatty, casts also sometimes presenting themselves. Occasionally in advanced and unfavorable cases of diabetes albuminuria may set in.

2. *A Disturbance of the Renal Circulation produced by an Extrarenal Cause, leading to Reduction or Increase of the Blood Pressure in the Kidneys.*—Diminished blood pressure in the glomeruli, as when brought about by pressure on the arteries, may cause albuminuria (RUNEBERG); but the experiments of GOTTWALT would make it appear that the higher the arterial pressure the greater should be the percentage of albumen. As Ludwig has pointed out, ligature or compression of the renal veins causes a great swelling up of the venous bundles in the marginal layer of the medulla of the kidney, which leads to a closure of the urinary tubules in the neighborhood. The disturbed circulation in the kidney may be produced by (*a*) compression of the renal veins by tumors or otherwise, or occlusion of these veins or of the vena cava ascendens by thrombi or emboli, or by an enlarged pregnant uterus (7th or 8th month, but occasionally in the 3rd or 4th month, 1 in 56—ARSDALE); (*b*) temporary compression of the renal artery; (*c*) increased arterial blood pressure in one kidney, caused by extirpation of the other or by compression of the aorta *below* the origin of the renal vessels; (*d*) compression of the aorta *above* the origin of the renal vessels (OVERBECK); (*e*) interference with the circulation from distension of the heart; (*f*) compression of the bronchi leading to convulsions, weakening of the cardiac beat, and suffocation; (*g*) great reduction of

temperature (LASSAR); (*h*) reduction of blood pressure, the quantity of the urine being at the same time diminished, as in cholera, in newborn children, in eclampsia parturientium, and occasionally in cases of epilepsy, tetanus, lead colic, and in many cases of chronic bronchitis, croupous pneumonia, phthisis pulmonalis, emphysema, pleurisy, and peritonitis: in many of these cases it would be difficult to state the true pathological cause and to say whether the renal pressure is reduced or raised.

The *congestion of the kidney* may be *active*, as in the temporary turgescence of the renal capillaries occasionally occurring in inflammatory and other fevers, after exposure to cold, in some forms of nerve irritation, and consequent on the passage of irritants through the kidneys; or *passive* and *secondary* to general venous engorgement of the kidneys, as in the venous obstruction resulting from cardiac, pulmonary, and hepatic disease, and in thoracic aneurism and mediastinal, ovarian, and other tumors.

Disturbed Innervation.—BERNARD found that lesions of different parts of the brain and spinal cord, as well as stimulation of the renal nerves, caused an appearance of albumen in the urine, the results being probably due to the alteration in the diameter of the blood vessels and in the blood pressure. In some nervous diseases the nervous symptoms may be associated with the renal disease, as in the hemiplegia resulting from cerebral hæmorrhage in contracted kidney with cardiac hypertrophy; or it may be a direct effect of the nervous disease itself, as in the temporary albuminuria occasionally observed after epileptic or other nervous fits, or in tumor of the brain or other cerebral lesions, as meningitis, tetanus, and delirium tremens (HUPPERT, FÜRSTNER, etc.).

4. *Alteration in the Constitution of the Blood*, brought about possibly by certain modifications in the tissue metamorphoses occurring in different febrile and inflammatory affections, as in a hydræmic condition of the blood with atony of the tissues, as occurs in purpura, scurvy, pyæmia, or after exhaustive illnesses and extensive alteration of important organs.—The injection of diluted and filtered white of egg into the veins of an animal is followed by its excretion by the kidneys; a similar injection of much water often leads to the same result. Want of common salt in the food, and an excess of a diet rich in albumen, especially after fasting, may also be succeeded by albuminuria. and occasionally in nursing women after sudden suppression of the secretion of milk albumen may appear in the urine.

Certain poisons may likewise lead to albumen in the urine, as the long-continued use of large doses of morphia, after deep chloroform narcosis, and the inhalation of arseniuretted hydrogen and carbonic oxide, etc., and in lead and phosphorus poisoning. The albuminuria occurring in cholera may depend on the increased specific gravity of the blood resulting from the profuse alvine discharges.

In many chronic and constitutional affections albuminuria may be noted, as in leukæmia, syphilis, cancer, scrofulous suppurations, etc., occasionally also in cases of chronic indigestion with constant alkaline urine or oxalate of lime deposits.

5. *Admixture of Blood, Pus, or Semen* with the urine may render it albuminous. The blood and pus may be derived from the kidney or

the urinary passages, bladder, etc. Look for blood or pus corpuscles, spermatozoa, threads of fibrin, and hæmoglobin. When a purulent urine is treated with liquor potassæ the deposit is rendered glairy or gelatinous.

Diagnosis.—It will readily be seen that in many of these cases the albuminuria is only *temporary*, as in zymotic diseases when there is a specific poison and a high temperature, and often in the course of such diseases as tubercle, cancer, and necrosis, etc.

In all cases of albuminuria it should accordingly be carefully noted whether or not the condition is a *temporary* or *permanent one;* an estimate should then be formed as to its amount; concurrent evidence should also be looked for, and note taken as to the quantity of the urine, its specific gravity, the presence in it of renal epithelium, tube casts, blood, pus, crystalline deposits, parasites, etc.

Above all the *student must not conclude, when he finds albumen in the urine, that its presence there is necessarily due to renal disease.*

A large amount of albumen in the 24 hours points to renal disease, and this is more likely to be the case if the urine is pale in color and of low sp. gr. (under 1012), and about 3 or 4 pints in quantity. As a rule a small amount of albumen and a dense and high-colored urine point to pyrexia, or to some interference with the renal circulation. Casts or renal epithelium are indicative of renal mischief. Therefore, if the urine is permanently albuminous, casts and renal epithelium present, and no other abnormal condition capable of producing the albuminuria to be detected, the probability is that the disease is renal.

It is of importance also in cases of albuminuria to determine the amount of urea passed, as the prognosis would, as a rule, be much more unfavorable if the excretion of this body fell considerably below the normal.

CHAPTER XXI.

HÆMATURIA—BLOOD IN THE URINE.

Blood is present in the urine in many diseases, the corpuscles and hæmoglobin, or in some cases the hæmoglobin alone. Fibrin or the fibrin generators may show themselves, in which case spontaneous coagulation would set in; but this is a very rare occurrence except in tropical countries.

Properties.—Urine containing blood, unless the amount is very slight, is either of a blood red or brownish color with a black, smoky, or greenish tint, and generally deposits a red or reddish brown sediment after standing. If the source of blood is other than the kidneys, as the ureters, bladder, or urethra, the color is of a brighter red, and clots are often present.

Tests.—1. *Presence of Blood Corpuscles, Casts, Renal Cells, etc.*—When blood is expected to be present the urine should be allowed to stand at rest for some time, to allow a deposit to be formed. The *microscope* detects blood corpuscles that may be almost unaltered, or much swollen, decolorized, and deformed; also blood and fibrin casts. At times microscopic examination fails to detect the corpuscles, on account of the changes they have undergone; recourse must then be had to the other tests. Much alteration in the corpuscles is likely to occur when the urine is ammoniacal or of very low specific gravity; otherwise, with the exception of some decolorization, they may retain their form for several days, and appear as circular, non-nucleated, somewhat flattened disks, which must not be confounded with sporules, discoid crystals of oxalate of lime, or renal epithelium. In cases of doubt, after examining the deposit upon a slide with the microscope, irrigate it with a strong watery solution of magenta (about 1 per cent.), which stains the nuclei of the renal epithelial cells and also the sporules; and irrigate in the same way another specimen with a solution of eosin (eosin 1, alum 1, alcohol 100), which imparts a rosy orange tint to the colored corpuscles, if they have not been completely deprived of their hæmoglobin. When the presence of the corpuscles has been satisfactorily established, it should be noted whether the blood is associated with calculi, parasites, or much mucus; and at the same time the observation carefully made whether or not the blood is intimately mixed with the urine, and blood, fibrin, or epithelial casts, or pus or cancer cells present.

2. *Presence of Hæmoglobin.*—The urine, according to HOPPE SEYLER, seldom contains oxyhæmoglobin, but instead methæmoglobin; with pathological urine containing blood, however, I have generally been able to obtain the absorption bands of oxyhæmoglobin, and sometimes that of the so-called methæmoglobin as well. The unfiltered urine should be examined directly.

(*a*) A layer of the urine is examined in a small glass vessel with parallel walls, the narrow slit of the spectroscope being brought into close proximity with it. Sometimes only the band near D is visible.

(*b*) If no absorption bands are seen add acetate of lead in excess to a considerable volume of the urine, filter, and shake up the precipitate thus obtained in a little water, where it is to be decomposed with sodic carbonate, then the precipitated lead carbonate removed by filtration, and the filtrate examined spectroscopically (HOPPE SEYLER).

(*c*) Mix in a test tube equal volumes of spirits of turpentine and tincture of guaiacum, freshly prepared by dissolving in alcohol (83 per cent.) small fragments detached from the interior of a large piece of the gum that has been broken in two. Shake this tincture and the spirits of turpentine well together, so as to form an emulsion; and add a little of the mixture to some of the urine in a test glass, pouring it slowly down the side of the tube upon the urine: if blood is present the resinous precipitate has more or less of a blue coloration (ALMEN).

Or the test may be thus made: Place a few drops of the urine in a test tube, add a drop of freshly prepared tincture of guaiacum, then a little ozonic ether, and shake well. If the ether rises to the surface of a blue color, blood is present.

3. *Presence of Hæmatin.*—(*a*) The urine is rendered strongly alkaline with caustic soda and boiled: the precipitated phosphates will be colored of a blood red by the contained hæmatin.

A somewhat similar reaction may be obtained with urine containing chrysophanic acid or the pigments of rhubarb or senna; but the deposit when treated with caustic potash, is not dichroic; and mineral acids, instead of brightening the color, as is the case with blood, render it less vivid.

(*b*) Acidulate the urine containing the blood with acetic acid and boil it, when a brownish coagulum of albumen and hæmatin is precipitated. Decant the urine from the coagulum, and having washed the latter with a little water, shake it up with some alcohol containing sulphuric acid: a red or reddish brown solution is thus obtained, which is to be filtered. If sufficiently concentrated it will show on spectroscopic examination a dark band midway between C and D, and another lighter and less decidedly marked but broader band extending from midway between D and E to F. Sometimes, however, with a certain degree of dilution this latter band may appear as two, one near F and the other near D. If now the alcoholic solution is evaporated to dryness and the residue incinerated, the presence of iron in the ash may be detected by dissolving it in a few drops of dilute hydrochloric acid, and adding a little ferrocyanide of potassium, when a blue precipitate is formed. This is best effected on a slide under the microscope.

4. *Presence of Hæmin.*—(*a*) By adding a few grains of chloride of sodium to the alcoholic solution obtained as in the last process, and evaporating it carefully, hæmin may be formed.

(*b*) Render the urine alkaline with ammonia or potash, then add some solution of tannic acid, and acidify with acetic acid. A dark precipitate is obtained, which is to be collected and washed on a filter, dried, and a little of it rubbed up in an agate mortar with a trace of sodic chloride, and then transferred to a test tube to which some glacial acetic acid is added, and the whole boiled; next filter into a watch glass, and dry the filtrate at a moderate temperature. Now heat the residue on a glass slide with some drops of glacial acetic acid, and having applied a cover glass heat again after the addition of more acetic acid; when cool examine under the microscope, and if blood has been present in the urine dark brown rhombic lamellæ of hæmin or flattended rhombic needles frequently crossed are to be seen (STRUVE).

To Distinguish between Hæmaturia and Albuminuria.—Bloody urine necessarily also contains albumen; hence it is often of importance to know, when blood is found in the urine, whether the whole of the albumen present comes from this source—whether, in short, the case is hæmaturia plus albuminuria or hæmaturia alone This can be ascertained by completely separating all the albumen from a definite volume of the urine, weighing it after it has been dried, and then incinerating and determining the iron present in the ash, from which the corresponding quantity of blood can be calculated.

Pathology.—The presence of blood in the urine indicates a hæmorrhage from some part of the uropoietic tract. Its causes and consequences vary greatly. It should be carefully noted whether or not the condition is permanent or temporary, in the former the prognosis being very unfavorable, as in cases of intense scurvy, septic fevers, etc.

Sources. 1. *Kidneys.*—Calculi, tubercle, cancer, or abscesses; in acute and occasionally in chronic forms of nephritis; aneurism and emboli of the renal arteries, and thrombosis of the renal veins; falls and blows leading to rupture; parasites in the mucous membrane of the pelvis, as in the endemic hæmaturia of hot climates, and in some cases of pyelitis; in the congestions at times occurring in the eruptive fevers, in which it may occur from the whole urinary tract; or as the result of exposure to cold, or after the use of cantharides, turpentine, and other powerful diuretics; occasionally also in a paroxysmal form, and in the hæmorrhagic diathesis often noted in scurvy, purpura hæmorrhagica, and malaria.

2. *Bladder.*—Diphtheritic and acute cystitis, calculi, carcinoma, congestion, fungoid growth, varicose veins, etc.
3. *Prostate.*—Structural disease.
4. *Urethra.*—After catheterization, etc.

Hæmoglobinuria.—Urine containing hæmoglobin without any blood corpuscles is of a very dark red color, coagulating on boiling and a brown scum forming on the surface. If it is now well shaken up with alcohol containing sulphuric acid the hæmoglobin is dissolved, and the alcoholic extract gives the absorption spectrum. This would point to hæmoglobin existing free in the serum of the blood, owing to a considerable destruction of the corpuscles in the blood vessels; and, indeed, it is possibly owing to the excess of hæmoglobin set free that it is excreted in the kidneys, for a small amount of this body is constantly being liberated under normal conditions. That this is very probable is shown by the result of experiments in which, when only small quantities of hæmoglobin were injected into the blood, no elimination of it occurred, whilst the injection of large quantities produced hæmoglobinuria (PONFIK).

This condition has been noticed after ingestion of excess of arseniuretted hydrogen, hydrochloric, phosphoric, lactic, sulphuric, and pyrogallic acids, and potassic chlorate and sodic bicarbonate; also at times after jaundice, fat, emboli, burns, typhoid fever, scarlatina, scurvy, putrid fevers, pernicious intermittent, transfusion of lamb's blood, etc.; and it has even appeared after long-continued cold baths and severe exercise.

Methæmoglobin is said to be frequently found in urine, appearing if much destruction of the colored corpuscles is induced in any way, as by injection of water, etc., or of blood of a different species, into the vessels. The urine is red, brown or black, and gives three absorption bands, of which the one between C and D, but nearer D, is characteristic. But if the urine is at all decomposed, or diluted with water and shaken some time in the air, the absorption bands of oxyhæmoglobin are obtained.

With few exceptions, when this body is present in urine, biliary acids are also to be found (HOPPE SEYLER).

CHAPTER XXII.

SUGAR IN THE URINE.

Melituria.—This combined with polyuria and polydipsia constitutes diabetes mellitus.

The weight of evidence, founded upon the reduction of cupric and bismuthic salts, and the evolution of carbonic anhydride when fermented with yeast, appears to be in favor of the opinion that a trace of sugar is generally found in healthy urine (BRÜCKE, MOSLER, ABELES, BENCE JONES, GUBLER, PAVY, IWANOFF, BÖDECKER), although many able observers have failed to separate grape sugar even from a large volume of urine (KÜLZ, MALY, MOSCATELLI, LEHMANN, LECONTE, SEEGEN, NEUBAUER, GORUP BESANEZ), while HAGER asserts that he can *always* find it in the urine of old people. Possibly, therefore, it may not always be present, but be affected considerably by different physiological conditions, such as the diet, etc. Indeed, there may be such a thing as an "alimentary glycosuria," as BERNARD termed it, produced by a food rich in sugars or starches.

Without entering into the vexed question of the source of the sugar found in the blood under normal conditions, further than to state that in the author's opinion the weight of evidence seems to favor BERNARD'S theory that it is in great part derived from the glycogen of the liver, we may safely say that in diabetes the amount of sugar in the organism is greatly increased, either from its excessive formation or from some hindrance to its decomposition when formed. Sugar is present in the blood, and we can readily see how easy it is for such a body to pass through the capillaries of the Malpighian capsules. In diabetes the venous blood has been found to contain 0·9 per cent. of sugar (HOPPE SEYLER); CANTANI has found 0·5 to 0·8 per cent. in the serum; but although it may amount to 10 per cent. in the urine it never rises in the blood above 1 per cent.; but this increased proportion of sugar in the blood can bring about diabetes, as we can prove experimentally, and in diabetes this increased formation of sugar is a constant factor.

Properties.—Diabetic urine is generally of a very pale straw color, often turbid, possessing frequently a slight greenish tint or a faint opalescence that increases as the urine stands. Its specific gravity is high (1030 to 1052, although very exceptionally it may be as low as 1005); its acidity is generally feeble, though occasionally excessive, often being neutral or feebly alkaline, and its odor is peculiar. Diabetic urine soon ferments with evolution of gas and production of sporules and filaments of the torula cerevisiæ, which generally collect after a time as a whitish deposit.

The *quantity* of urine seldom sinks below 3½ pints in the twenty-four hours, but it varies generally between 8 and 15 pints, although it may be much greater. The occurrence of fevers or inflammations diminishes it greatly. 4 per cent. is the average amount of sugar present, rarely rising much above this, but it may form 12 per cent.

Sugar of milk may be found in the urine when the secretion of milk or its discharge is suddenly arrested; this is a regular occurrence 24 to 48 hours after weaning.

An *acetone body* is also occasionally present in diabetic urine, which gives a brownish red coloration with ferric chloride; such patients frequently emit an odor of acetone in the breath.

Tests. 1. TROMMER'S.—Add to the urine one-fourth to one-third its volume of caustic soda solution, then drop by drop a solution of cupric sulphate (1 : 10) until the precipitate formed appears to have dissolved completely; heat the upper third of the mixture in the test tube, and a *yellowish red precipitate* is formed before the boiling point is reached.

Or apply the test by dropping the urine slowly into a little boiling diluted Fehling's solution until rather less than an equal volume of the urine has been added. If very little sugar is present 5 to 20 minutes may elapse before the suboxide is deposited; the boiling, however, is not to be prolonged. But a milky appearance is very suspicious, and generally indicates sugar.

Uric acid, hypoxanthin, and mucus, etc., possess a reducing action on cupric oxide; the reduction also by sugar is more or less hindered by the presence of albuminous bodies, peptone, pepsin, kreatin, kreatinin, and to a less degree by the urinary pigments in excess.

Sometimes the reaction fails unless the urine is diluted before being tested (KÜLZ). The presence of reducing agents in the urine other than sugar may give rise to a strong yellow coloration after the urine has been boiled with the cupric oxide and set aside for a few minutes. In case of doubt lay aside a similar mixture *in the cold* for twenty-four hours, and the suboxide will separate if sugar is present. Or, where there is very little sugar present and some doubt as to the cause of the reduction of the cupric oxide, the urine may be precipitated with plumbic acetate and the filtrate tested with the Fehling's solution.

If there is very little sugar it is advisable to filter the urine through animal charcoal several times, and the resulting limpid filtrate will give the sugar reactions more sharply, although a little of the sugar is retained by the charcoal (SEEGEN).

2. *Circular Polarization.*—A urine containing even 0·3 per cent. sugar will give a marked polarization to the right. Diabetic urine is generally sufficiently clear for the purpose; but if too highly colored it should be filtered through animal charcoal, although charcoal is not to be highly recommended, as it holds back some of the sugar; better therefore to precipitate the coloring matter with neutral lead acetate, and to pass the urine through an unmoistened filter into a dry beaker. If albumen is present it must be separated, as it polarizes the light differently to sugar—that is, to the left. Take 100 c.c. urine, add a drop or two of acetic acid, and boil for some time; filter and wash the precipitate with water until the filtrate occupies exactly 100 c.c. When cold test with the polariscope.

The use of chloral and of certain aromatic bodies interferes with this process, on account of their presence in the urine causing polarization to the left.

3. *Fermentation Test.*—Add a little washed yeast to a long, narrow, closed tube, then fill this up with the urine and invert over water or mercury. Lay aside for 12 hours in a moderately warm place, and then note the accumulation of gas in the tube and the consequent displacement of the urine. The gas may be shown to be carbonic acid by its extinguishing a burning taper when dipped in it, and by forming an opalescent fluid when shaken up with lime water.

4. *Bismuth Test.*—According to BÖTTGER no other body present in urine except sugar reduces the bismuth salt.

Make a solution of carbonate of soda (1 to 3 water); mix a little of this and the urine in equal volumes, and then add a pinch of basic bismuthic nitrate; now boil for a few minutes: the presence of sugar is shown by the bismuthic salt becoming reduced and a grayish or blackish deposit or coloration produced (see p. 79).

If much pigment or albumen is present separate the latter by acidifying with acetic acid and boiling, and the former by filtration through animal charcoal.

5. When only traces of sugar are present SEEGEN'S plan of repeatedly filtering the urine through animal charcoal until it is colorless, then washing the charcoal with a little distilled water, and testing the washings with a little Fehling's solution, may be adopted with advantage.

6. In case of doubt, and if we wish positive proof of the presence of sugar, filter the urine through animal charcoal and evaporate to a syrup; digest the residue with alcohol (82 per cent.), evaporate the alcoholic solution, and apply Trommer's test to the residue dissolved in water. Test also the washings of the charcoal as above.

7. *Torulæ* are developed in diabetic urine, the yeast fungus and the penicillium glaucum. A white scum, due to these bodies and highly characteristic of the presence of sugar, soon accumulates on the surface. They generally occur as minute oval vesicles that change their shape by growing and developing new vesicles.

8. *Clinical Method* (PRATESI, *after* HORSLEY).—Dissolve caustic potash 2·5 grams in 60 grams very concentrated liquid potassic silicate, and then add 2 grams potassic bichromate. Preserve this solution in a well-stoppered bottle. Now cut a piece of tin into strips about three inches long and a little more than one-third inch wide. With a glass rod place a drop of the above solution on the end of one of the strips of tin and dry it there at a gentle heat; two, three, or more drops are also to be dried at the same spot. To test for sugar one of these prepared slips is to be taken and the deposit heated, when it swells up and takes a canary-yellow color. Drops of the urine are now to be placed over the yellow deposit one at a time, heating after each addition, so as to evaporate almost to complete dryness. If sugar is present and in a proportion not less than 0·4 to 0·5 per cent., a *green coloration* shows itself, owing to the reduction of the chromate by the decomposition products of the sugar.

9. *Picric Acid Test.*—Add to the urine an equal volume of a saturated watery solution of picric acid, and after the subsequent addition of a little caustic potash heat gently, when a *marked reddish brown coloration* will show itself. This change of color is due to the formation of picramic acid.

By means of this color test Dr. G. JOHNSON makes a quantitative estimation of the sugar present in a diabetic urine. A standard of comparison is first prepared by adding to a long test tube one drachm of a solution of grape sugar containing one grain to the fluidounce, half a drachm of liquor potassæ (B. P.), ten drops of a saturated solution of picric acid, and distilled water up to half an ounce; this mixture is then raised to boiling point, and the boiling continued for a minute. A claret red color is developed, and its depth of tint indicates a quarter grain of sugar to the fluidounce. But, as the tint becomes paler after a few hours, it is advisable to imitate it by adding acetic acid to a solution of ferric chloride, and to enclose the resulting fluid in a stoppered bottle, so as to serve as a permanent standard of comparison.

The process consists in boiling for a minute a mixture of a drachm of the saccharine urine, half a drachm of liquor potassæ, and twenty drops of a saturated solution of picric acid, the whole being made up to half an ounce with distilled water. According to the amount of sugar present will be the intensity of color produced. Two small, vertically arranged tubes are now to be placed in a good light on white paper; into one of them is poured some of the standard of comparison, and into the other the more or less diluted colored solution obtained by boiling the urine as above with the picric acid and potash. The dilution is to be made in a graduated tube, and it is to be repeated until equal columns of the diluted solution and of the standard of comparison exhibit the same tint when examined vertically in a good light. After each comparison the colored urine must be returned to the graduated tube in which the dilution is effected, until the process is completed; and from the amount of dilution required the proportion of sugar present is calculated.

To Separate the Sugar from the Urine.—Evaporate the urine to a syrupy consistence and let it stand aside, when after a time yellow, friable masses of sugar will crystallize out—a process that may be favored by treating the syrup with ether and then letting it evaporate. Digest the residue with absolute alcohol to remove the urea and extractives, and separate any sodic chloride present by dissolving the crystals of sugar in water and precipitating with sulphate of silver; then filter, evaporate, and digest the residue with spirit to dissolve up the sugar.

Quantitative Estimation. I. *By* FEHLING'S *Method.*—See p. 87.

The method has thus been modified and greatly simplified by Dr. DUHOMME: Two small pipettes, graduated to deliver 1 and 2 c.c. respectively, are required, as well as two or three test tubes. A preliminary experiment is first required to ascertain the number of drops in a c.c. of the urine to be tested: this is readily effected by drawing up a c.c. of the urine into the graduated pipette, and then allowing it to escape in drops.

2 c.c. of Fehling's solution are diluted in a test tube with an equal volume of liquor sodæ and boiled. Titration is next performed with the diluted urine as in FEHLING'S process. The number of drops found to be contained in 1 c.c. of the urine multiplied by ten, and the product divided by the number of drops of the urine required in the titration, equals the amount of glucose per litre in grams.

II. *By Circular Polarization.*—Fill the two-decimetre tube of the polariscope with the filtered urine, and having rendered the tint alike in both halves of the double plate, read upon the scale and vernier the deviation in degrees. When the two-decimetre tube is used the percentage in grams is obtained by dividing the number of degrees by 2, while with the one-decimetre tube the number of degrees represents directly the percentage of sugar in the urine. (For full details of the process see p. 83.)

If albumen is present it must first be removed by adding a drop or two of acetic acid and boiling some time, or before boiling adding an equal volume of saturated sodic sulphate solution in addition to the acetic acid; the filtrate is ready for testing.

The estimations by circular polarization do not always agree with those obtained by FEHLING'S method, which is due probably to the presence of other bodies allied to sugar.

III. *Approximative Estimation from the Density* (Bouchardat).—Having ascertained the presence of sugar, determine the density of the urine exactly with a urinometer, and ascertain how much is passed in the 24 hours; or it is better to collect the whole urine passed in that time, and take the density of this. Suppose the total amount to be 4 litres, and the density at 15° $= 1036$. An approximation to the amount of solids in urine is obtained (see p. 329) by multiplying 36 by 2, and for 4 litres this would be $36 \times 2 \times 4 = 288$ grams solids; and taking 50 grams as the average weight of solids of healthy urine, $288 - 50 = 238$ grams of sugar would accordingly be present in the 4 litres passed in the 24 hours. As, however, the urea as well as some of the other urinary constituents are also greatly increased in diabetes, this estimation can only be regarded as a very rough approximation.

If in the determination of the density the temperature of the urine is above or below 15° (for which temperature the urinometer is generally graduated) a correction must be made as follows:—

Subtract from the degree obtained. Temp.		Add to the degree obtained. Temp.	
0° to 5°	1·3	16°	0·2
6°	1·2	17°	0·4
7°	1·1	18°	0·6
8°	1·0	19°	0·8
9°	0·9	20°	1·0
10°	0·8	21°	1·2
11°	0·7	22°	1·4
12°	0·6	23°	1·6
13°	0·4	24°	1·9
14°	0·2	25°	2·2

This method serves better when there is an abundant secretion of urine rather than when it is comparatively scanty.

Pathology.—When sugar has been detected with certainty in the urine the next important step is to *ascertain if its presence there is only temporary or if it is constant;* then it is desirable to find out the amount daily excreted and also the quantity of fluid discharged.

Permanent glycosuria constitutes diabetes mellitus. In this disease not only is sugar present in the urine, and occasionally in the sweat and other secretions, but there is generally also an increased discharge of water, urea, and phosphates, the fixed salts like sodium chloride and the like being generally diminished, while less carbonic anhydride is expired and less oxygen absorbed than in health (Voit). While heredity seems to be a prominent factor, mental distress, an excessively saccharine diet, and gout appear to act as determining causes. In many cases where the quantity of urine passed is small there is abundant perspiration. A diminution in the amount of sugar often coincides with an increase in the phosphates and oxalates. The albumen sometimes present in the urine is frequently an evidence of renal disease (Rayer), its amount often having been observed to be related inversely to that of the sugar (Schmitz). The muscular weakness that is often present is said to be due to a general alteration in the muscular fibres, extending even to the cardiac muscle. Death may therefore be due not only to diabetic coma and acetonæmia, but also to cardiac weakness.

Transitory glycosuria, on the other hand, may show itself in the early stages of tetanus, cerebrospinal meningitis, cases of cerebral apoplexy, tumors of the medulla oblongata and of the pia mater, particularly in the fourth ventricle; in chronic inflammatory changes in the calamus scriptorius, carcinoma of the pituitary gland, cerebral softening and atrophy of the gray substance; in myelitis, general paralysis, and sometimes after epileptic fits or direct injury by blows or shocks to the brain and sympathetic, and occasionally after over-work; in some heart and lung affections, as pneumonia and phthisis, after paroxysms of whooping cough and spasmodic asthma; occasionally in cirrhosis of the liver, as a result of different disturbances of the abdominal circulation, and freqently when the secretion of the mammary glands is hindered (SINÉTY); at times also when carbuncles are present, and in the urine of pregnancy, cholera, intermittent fever, gout, and Bright's disease.

Artificial Production of Diabetes.—The appearance of sugar in the urine can be brought about by puncturing the medulla oblongata in the vasomotor area, a little above the point of the calamus scriptorius and behind the corpora quadrigemina, but for this to be successful the olivary fasciculi should be injured (BERNARD). The same result can also be produced by puncturing other parts of the nerve centres, as by destroying the spinal cord at the origin of the brachial nerves and opposite the second dorsal vertebra (SCHIFF), by division of the sympathetic in the thorax; also by impeding the respiration (PAVY), or injecting different bodies, such as dilute phosphoric acid, much 1 per cent. sodic chloride solution, inulin, or arterial blood (PAVY), into the portal vein.

Most of the injuries that are followed by sugar in the urine appear to produce hyperæmia of the liver. Further, sugar may appear in the urine after large doses of strychnine, morphia, curara, chloral, amyl nitrite, spirits of turpentine (ALMÉN), deep chloroform or ether narcosis, carbonic oxide poisoning, subcutaneous injection of nitrobenzol or nitrotoluol, and copious ingestion of lactic acid. In arsenical and phosphorus poisoning, although the liver becomes diseased and is said to contain no glycogen, yet sugar is found in the urine. Ligature of the bile ducts also causes the glycogen to disappear (LEGG).

Temporary glycosuria may likewise be induced by an alimentation too rich in starch and sugar, especially after long abstinence; and this is more liable to occur with a diminished alkalinity of the blood and an enfeebled respiration; an injection of concentrated solution of sugar of milk into the stomach leads to the same result.

The reducing body found in the urine in all these cases, however, may not always be sugar.

The different cases given above of transitory glycosuria may, from their nature and results, be classified into—

1. *Temporary or incidental*, as in those occurring after deep chloroform narcosis, after excessive ingestion of saccharine and amylaceous food, in asthma, epilepsy, and in the convalescence of cholera, etc.

2. *More or less permanent*, as in true diabetes: (*a*) flow of urine increased, with abundance of sugar, and associated with thirst, debility, emaciation, etc.; (*b*) sugar slight or considerable, persistent or intermittent in its appearance, but without any serious attendant symptoms.

Alkapton and *pyrocatechin* are occasionally, but rarely, present in urine; they give some of the same reactions as sugar, but they do not reply to the bismuth or fermentation tests. *Alkapton* is obtained by precipitating the urine with acetate of lead, filtering, precipitating the filtrate with basic lead acetate, and collecting the precipitate; this precipitate is washed, suspended in water, and decomposed with hydric sulphide; the filtrate is evaporated to dryness and extracted with ether. It is a golden yellow, resinous body, very deliquescent, and soluble in water and spirit; it becomes brown when exposed to the air, and the urine containing it may produce brown stains on linen.

CHAPTER XXIII.

BILIARY URINE.

THE biliary acids being generally in great part reabsorbed and disposed of in the blood under normal conditions, most probably being chiefly oxidized to the state of carbonic acid and water, we can easily understand that obstruction to the escape of the bile produces a greater effect from the retention of the pigments, of which normally so much is excreted with the fæces, than from the retention of the biliary acids; so that we may only expect to meet with them when there is a hypersecretion of bile. But according to DRAGENDORFF, NAUYN, and VOGEL the biliary acids in minute proportion, as well as traces of the pigments, are normal constituents of urine; but they are often entirely absent (HOPPE SEYLER, KÜLZ).

The amount of biliary acids excreted is very slight, for while RANKE calculated that about 10 grams are formed in the 24 hours, not more than one-third of a gram has been found in the urine passed in that time in cases of jaundice. Whether or not the biliary pigments are generally present is doubtful, but they are certainly occasionally present in the urine of healthy persons in summer time (SCHERER); in jaundice they are a common constituent of the urine, while in intense forms of this disease they may be present in all the fluids of the body.

Properties.—The urine is of a yellowish brown to a greenish tint, the color becoming darker on exposure to the air; it froths readily, and the froth is of a characteristic deep yellow color. The ingestion of santonin and chrysophanic acid give a somewhat similar color to the urine.

Tests. A. *The Biliary Acids.*—The detection of the biliary acids is much more difficult than that of the pigments; and the presence of much pigment, of oxidizing substances, or of albumen, etc., interferes with Pettenkofer's reaction.

1. PETTENKOFER'S *Test.*—(*a*) Shake a little of the urine with a drop of syrup, and then allow the sulphuric acid to trickle down the side of the inclined test tube. Note the purple band at the upper margin of the acid.

The sulphuric acid must not contain sulphurous acid, and the temperature must not be allowed to rise much above 38° C.; albumen also must be separated if present. The presence of different essential oils may produce the same coloration (see p. 182).

(*b*) Dissolve a little cane sugar in the urine and dip into it a piece of filter paper, which is then removed and left to dry. A drop of strong sulphuric acid is added to this by means of a glass rod, and in a quarter of a minute a violet red spot generally shows itself. The method is delicate (STRASSBURG).

(*c*) The froth test may also be applied (CHARLES). See p. 178.

2. It is always advisable, in case of doubt, to isolate the biliary acids before applying the test.

(*a*) HOPPE SEYLER thus proceeds: Precipitate the urine with acetate of lead and a little ammonia, wash the precipitate on a filter with water, and then, having boiled it with alcohol, filter hot. The hot alcohol dissolves the lead salts of the biliary acids. This hot filtrate is treated with some drops of carbonate of soda solution and evaporated to dryness over a water bath: the residue is extracted with boiling absolute alcohol; this last extract is to be collected in a closed flask, and a little ether added, the alcoholic solution being first concentrated to a small volume if necessary. A resinous precipitate soon falls, which may become crystalline if allowed to stand long enough under ether, but a solution of the resinous precipitate serves for the test.

(*b*) Another plan of isolation is SALKOWSKI'S. The urine is first evaporated and the residue extracted with spirit, the spirituous extract diluted, and the precipitate taken up again with absolute alcohol. By diluting the last alcoholic extract a precipitate is again obtained, which is to be dissolved in water and treated with acetate of lead and a little ammonia, as in HOPPE SEYLER'S process.

(*c*) Evaporate the urine, treat the residue with alcohol, and evaporate the alcoholic filtrate. A few drops of water are then rubbed up with the dried extract, and a solution of sugar in water (1 in 3) mixed with it. Strong sulphuric acid is next added drop by drop, and a purple color will soon appear, which, however, quickly fades. Too much water and a temperature above 60° interfere with the reaction.

(*d*) HOPPE'S *Method.*—Treat the suspected urine with excess of milk of lime and boil for half an hour or so; filter, evaporate the filtrate nearly to dryness, add excess of hydrochloric acid, and boil for another half-hour, adding fresh acid from time to time. Dilute when quite cold with five to six times its volume of water, filter, and wash the resinous mass obtained, which is then to be dissolved in absolute alcohol, treated with animal charcoal, again filtered, and the filtrate evaporated to dryness. *Choloidic acid*, a derivative of the biliary acids through cholic or cholalic acid, is thus obtained. It is dissolved in a little caustic soda and warm water, a drop or two of syrup added, and a few drops of sulphuric acid allowed to trickle slowly into the mixture; a dark violet color is produced.

B. *The Biliary Pigments.*—The urine must not be allowed to decompose before the examination for pigments is made; otherwise hydrobilirubin may have replaced the bilirubin or biliverdin.

1. GMELIN'S *Test*, which depends on the play of colors produced by the oxidation of the pigment by means of nitric acid, can be performed after many methods.

(*a*) That commonly employed is to spread a few drops of the urine on a white plate, and then to bring a drop or two of yellow nitric acid in contact with the margin of the thin layer of urine or into its middle: the play of colors that appears at the point of contact commences with green and ends with red and yellow.

The nitric acid should contain a little nitrous acid, which is easily effected by heating it with a piece of stick or a fragment of sugar; but too much nitrous acid is to be avoided.

(*b*) Pour some strong yellow nitric acid into a test tube, and let the urine trickle down the side of the tube upon it; a green band first appears at the point of contact of the two fluids, which extends higher and higher, and is succeeded inferiorly by a blue, a reddish violet, and a yellow layer, and of these the green and the red are most characteristic (KÜHNE).

(*c*) After filtering the urine pour the nitric acid over the inner side of the filter; the play of colors is well marked. If the filter is allowed to dry the reaction succeeds better. Merely dipping the filter paper in the urine produces less intensity of color (ROSENBACH).

(*d*) Mix the urine with very dilute nitric acid, and then let strong sulphuric acid run down the side of the test tube: the colored rings spread from the upper surface (BRÜCKE).

(*e*) Add a little albumen to the urine before the nitric acid: the albumen is precipitated of a dull green or bluish color (HELLER).

(*f*) Tested with an alcoholic solution of bromine (5 per cent.) and with aqueous chloric and iodic acids (20 per cent.), three stages of coloration are obtained—green, blue, and violet—after which there ensues a change of color to reddish, yellow, and finally decoloration.

Fallacies of GMELIN'S *Test.*—The presence of alcohol and indican may give indications that are liable to be mistaken for those of bile, but note that with indican only red and violet zones will show themselves, while with bile pigment, unless the solution is very dilute, the zones are all present in the order already given, green appearing first. To avoid any difficulty from indican add to a little of the urine some drops of a solution of potassic nitrate and a few drops of sulphuric acid: a beautiful green color is produced by traces of bile; but the color rapidly disappears, becoming yellow.

2. If a solution of *violet of methylanilin* is poured into normal urine, a blue ring will be formed at the surface of the liquid, but if the urine is icteric the ring is of an *intense carmine color*. This only occurs with icteric urine, and not with normal urine to which bile has been added, nor with urine containing other coloring principles (PAUL).

3. Sometimes bile pigment may be present in urine and yet not give the color reaction; this is more frequently the case with the urine of patients whose temperature has continued high for some time (PRUSSAK). In such urines we therefore require to *separate the pigments* before testing. This may be effected by one of the following processes, to one of which in cases of doubt it is advisable to have recourse, as by doing so we avoid any mistake from the presence of methæmoglobin, urobilin, or indican, etc.:—

(*a*) Precipitate the urine with milk of lime and transfer a piece of the precipitate, the size of half a hazel nut, to a test glass; wash it here several times with water to remove any indican that may be present; then half fill the tube with absolute alcohol and render distinctly acid with dilute sulphuric acid. It is next warmed and filtered, and on boiling the filtrate the biliary pigment will show itself by the appearance of a dark green to a blue coloration, though in some cases it remains yellow or greenish yellow [here choletelin only may be present (HEYNSIUS), so we must acidify with hydrochloric acid and examine spectroscopically.] The bilirubin is precipitated by the lime, from which combination it is liberated by the sulphuric acid, and is then dissolved up by the acidulated alcohol (HUPPERT).

(*b*) HOPPE SEYLER precipitates with milk of lime as above, but to effect complete precipitation he passes a current of carbonic acid through the liquid. The precipitate is let stand several hours, then collected on a filter and shaken up in some water to which chloroform and acetic acid have been added. The chloroform solution is either yellow or green, according to the excess of bilirubin or of biliverdin, and to it GMELIN'S test can be applied.

(*c*) SALKOWSKI proceeds thus: Render the urine alkaline with a little sodic carbonate, and add calcium chloride solution drop by drop and with repeated shaking until the supernatant liquid is of the color of normal urine. Collect the gelatinous precipitate, wash it well, and having transferred it to a small flask, cover it with alcohol, and dissolve it by shaking well with a little hydrochloric acid. On boiling the clear solution it will become of a green to a blue color, changing to a violet or red on the addition of nitric acid.

(*d*) The pigments may be precipitated with basic lead acetate, the precipitate decomposed with hydric sulphide, then washed with water, and the pigments finally extracted with chloroform.

(*e*) An easy method, which succeeds often when the urine gives no evident reaction of biliary pigment, is to place the urine in a freezing mixture for some time until the urates have separated, then to collect these on a filter and dissolve them in hot water; this solution will give the characteristic pigment reaction.

(*f*) Acidify a large quantity of the urine with a little acetic acid, and then shake it up well with chloroform added a little at a time; allow the urine to stand and decant the supernatant chloroform, which can be used to extract fresh quantities of urine until it is well colored. The chloroform is next thrown on a filter and washed with water; it passes through, and even with traces of bilirubin presents a yellow color. Test portions of this chloroform extract as follows:—

(1) By shaking with carbonate of soda we obtain an alkaline solution of the pigment, to which the ordinary nitric acid test may be applied, or the chloroform solution may be tested directly.

(2) Dilute the chloroform solution or evaporate a little on a slide, and bilirubin will be obtained in microscopic crystals. The color reaction can also be well seen under the microscope by treating the crystalline residue with nitric acid.

(3) Carefully pour a few drops of yellow nitric acid over a little of the chloroform extract in a test glass: the play of colors is seen.

(4) Treat with ozonized spirits of turpentine or with a trace of watery solution of iodine in potassic iodide: a green color appears.

(5) Shake a little some time with caustic potash, and a greenish solution of biliverdin is obtained.

(6) The addition of a strong sulphuric acid gives a green coloration.

(7) Treat a little with bromine water, and a series of colored rings will be formed.

(*g*) By shaking the urine with ether the latter is colored yellow. Pour this ether into a test tube and hold it over the mouth of a flask filled with strong bromine water: the ether will gradually assume a blue color.

Pathology.—The presence of the *biliary acids* in urine has been denied by several chemists, but HOPPE SEYLER has found them in more than 30 cases of jaundice, a fact which has so frequently been substantiated since that we may look on it as proved. But undoubtedly to obtain characteristic evidence of their presence in urine they must first be separated. These biliary acids are present and increased in some cases of jaundice and acute atrophy of the liver, and occasionally in pneumonia; but their presence or absence is not of so great importance as some authors (Harley, etc.) have supposed, although their presence may at least indicate an accumulation of them in the blood, and consequently, if excessive, a tendency to paralysis of the nerves, particularly those of the heart (Ritter, etc.)

The biliary pigments in excess will accompany the biliary acids after obstruction of the bile ducts, and especially when the jaundice coincides with acute inflammation or atrophy of the liver; in certain disturbed states of nutrition also, as in starvation, diabetes, and after phosphorus poisoning and snake-bite, both bodies may present themselves in the urine, but with the pigments biliverdin and biliprasin generally predominating (Vogel).

If the liver is at all inactive in its functions, from disease or otherwise, it can easily be seen that an accumulation of pigment is likely to occur. This retention of pigment is often to be seen in degenerative changes of the liver and weakening of its blood stream; as the result of the ingestion of ether, chloroform, or arseniuretted hydrogen; also in severe infective diseases, as in typhus, malaria, pyæmia, septic poisonings, and multiple abscess of the liver.

The different forms of jaundice may be classified according to their origin into *absorption*, *aspiration*, *and suppression icterus*, together with what has been called *blood icterus*.

1. By a closure of the bile ducts the bile accumulates, followed by its reabsorption (*absorption icterus*). This may occur in catarrhal jaundice, carcinoma of the liver, nutmeg and syphilitic liver, cirrhosis of the liver, closure of the ducts by calculi, etc.

2. In other cases a sinking of the blood pressure in the liver leads to the same result (*aspiration icterus*), as in pylephlebitis and icterus neonatorum. The reabsorption may arise either from *diminished pressure in the blood vessels*, as in this form of jaundice, or from *increased pressure in the bile ducts*, as in jaundice from absorption.

3. The term *suppression icterus* is applied to the jaundice due to the cessation in the production of the biliary constituents in the liver and their accumulation in the blood through a deficient excretion.

4. In the form of jaundice to which Virchow has applied the term *blood icterus* there appears to be an increased decomposition of the corpuscles and a liberation of hæmoglobin, which forms the source of a greatly increased production of bilirubin. From hæmoglobin is derived the hæmatoidin of old extravasations, and this latter body is regarded as identical with bilirubin (Jaffé, Heidenhain). A solution of hæmoglobin injected into the blood causes jaundice and a separation of biliary pigment in the urine. Injection also of bodies that tend to dissolve the corpuscles, such as water, ether, chloroform, and biliary acids effects the same thing.

CHAPTER XXIV.

MUCUS AND PUS; CHYLURIA.

Mucus in small quantity is a common constituent of the normal urine, forming a faint, flocculent, transparent cloud that deposits after a time.

Vesical mucus is semitransparent and rich in corpuscles and epithelium, and, if the urine is alkaline, also in oxalate of lime and triple phosphate crystals. It is frequently found in urinary sediment and must not be confounded with albumen; nor must the long cylinders or filaments of mucus that are often to be met with be mistaken for urinary casts.

MUCUS is precipitated by the mineral acids, but it is soluble in excess. It differs from pus in not being precipitated by neutral acetate of lead, which precipitates the pyin of pus.

To detect it in urine treat a portion of that fluid with twice its volume of alcohol (95 per cent.), filter off the precipitate, and wash it in water. The urine is also rendered slightly cloudy by the addition of acetic acid, in which mucin is not soluble. A simple filtration of urine will not remove all the mucus, as mucin, it should be remembered, is soluble in a large quantity of water as well as in a slight excess of the mineral acids.

To determine its amount dilute the urine (about 300 grams) with twice its volume of water and acidify strongly with acetic acid; then cool to 5° or 6°, filter, and wash the precipitate with a little dilute acetic acid. It can thus be separated from albumen; but if any pus or blood is present redissolve the precipitate in water slightly acidulated with hydrochloric acid, and saturate the solution exactly with caustic soda; then reprecipitate the mucin by adding a few drops of acetic acid, and weigh it on a tared filter after it has been washed with alcohol and ether and dried.

The thick glairy deposit occasionally formed by pus must not be mistaken for mucus. In the former case the urine is alkaline and crystals of triple phosphate are present. Mucus is specially abundant in catarrh or inflammation of the bladder or urethra; numerous imperfectly formed mucus cells are then present with much epithelium.

PUS may show itself in the urine in very small amount or as a bulky deposit resembling urates. The urine containing it is generally turbid when voided, and it soon deposits a dense yellowish white sediment. Some time after the urine has been passed the pus often assumes a slimy, ropy, viscid, and tenacious character, swelling out against the sides of the vessel, and capable of being drawn out into long tough strings. This ropiness is generally due to the action upon it of ammonia developed by the decomposition of urea. The same thing can also be effected by the addition of caustic potash. This reagent serves at the same time to distinguish it from pale urates, which are thus dissolved.

When examined under the microscope the corpuscles appear as little granular globules, varying somewhat in appearance with the reaction of the urine; they are cleared up by dilute acetic acid, a folded or cleft tripartite nucleolated nucleus coming into view at the same time. Blood corpuscles and triple phosphate crystals may also be present, and croupous shreds, especially after irritant diuretics.

Source of the Pus.—Pus may appear in the urine in renal embolism, renal abscesses, suppuration of the pelvis of the kidney, discharge of pus from pelvic, perinephritic, and other abscesses, inflammation or cancer of the bladder, and suppuration of the prostate or urethra. In women the pus may have a vaginal origin and be due to leucorrhœa.

The character of the admixed cells should be carefully ascertained, and the way in which the pus comes away should be noted—whether more abundant at the beginning of the act of micturition, as in urethral disease, or towards the end, as in cystic disease. When the pus comes from the kidney the urine is generally acid when passed, but when it is derived from the bladder the reaction is usually ammoniacal, especially if the suppuration is of old standing. In vesical pus too blood, if present, is mixed up with the mucus and pus, while in renal suppuration the blood lies usually on the top of the pus.

Albumen can always be detected in the urine if much pus is present, as by boiling, precipitation with mercuric chloride, acetic acid and potassic ferrocyanide, but generally only a haziness on the addition of nitric acid. It is therefore sometimes a matter of difficulty to decide as to its origin, for albumen may be present also as a result of kidney disease. The diagnosis must here depend on the amount of the albumen relative to the quantity of pus, on the presence of casts, calculi, crystalline deposits, etc.

CHYLURIA.—In this condition a milky and fat-holding urine is excreted. The quantity and specific gravity of the urine remain about normal, the color, however, being milky white to yellowish red, the reaction neutral or weakly acid, but easily becoming alkaline; on standing a white layer may accumulate on the surface, or a coagulum may show itself. The white supernatant layer consists of very finely divided fatty particles, as can be shown with ether and acetic acid; and in the sediment a few lymph cells or blood corpuscles may be met with. The presence of fine embryonic worms (*filaria sanguinis*) was discovered by LEWIS not only in the urine, but also in the blood and the tissue of the kidney. Some have maintained the existence of abnormal communications between the lymphatic vessels and the urinary passages. The blood has also been seen to be very rich in fine free molecules (SCRIBA), which are said to find a passage through the membrane of the glomerulus.

Very characteristic is the alteration often presented by the urine, the chylous aspect occasionally disappearing and reappearing very rapidly.

In addition to the ordinary urinary constituents, fat, lecithin, cholesterin, and albumen have been obtained in chylous urine. The fat is generally under 1 per cent., though more may be present. Different observers have also detected the presence of small quantities of glycerophosphoric acid, peptone, sugar, phenol, and indican in different specimens. Fat and fatty matters, it may be said, are extremely rare in the urine; but, in addition to chyluria, an admixture of a large quantity of pus with the urine may lead to their presence; fat is also occasionally present in fatty degeneration of the kidney and in acute phosphorus poisoning; but rarely in fatty degeneration of the epithelial cells of the urinary passages.

To separate fatty bodies from urine a large quantity of this fluid is treated with ether, with which it is well shaken, then rendered alkaline with caustic soda, and again shaken up with more ether; this ethereal extract is distilled and the residue taken up in pure ether. The amount may be determined in this way by weighing the residue of the last ethereal extract.

The presence of cholesterin in this residue may easily be recognized by shaking it up with an alcoholic solution of caustic potash and then with ether, which latter dissolves the cholesterin and only a little of the soap formed. By evaporating the last extract we obtain the characteristic thin rhombic tables, to which the tests for cholesterin can be applied.

CHAPTER XXV.

ADDITIONAL ABNORMAL CONSTITUENTS.

EXCRETION BY THE KIDNEYS OF MANY ORGANIC AND INORGANIC SUBSTANCES, AND THE MODE OF DETECTING SOME OF THEM.

A sulphocyanide is said to be present in the urine of smokers. *Sulphuretted hydrogen* has been noticed in cases of tuberculosis, variola, cancer, and enlargement of the bladder. *Lactic acid* has been met with in acute atrophy of the liver, and in leukæmia, rickets, osteomalacia, and trichinosis; *sarcolactic acid* in acute phosphorus poisoning. Such fatty acids as formic, propionic, and butyric have likewise been observed.

A great many bodies when taken are excreted by the kidneys almost unaltered, while others may be only slightly changed.

I. Inorganic Substances.

1. The *neutral alkali salts*, as the chlorides, bromides, and iodides, appear unaltered in the urine.

2. The *alkaline carbonates* diminish the acidity of the urine, or render it alkaline. The carbonate of ammonia appears as urea, and does not influence the reaction. *Salts of cæsium, rubidium, lithium*, etc., also appear quickly in the urine; likewise potassic ferrocyanide.

3. The *alkaline earths* are discharged in the urine only in small proportion.

4. *Salts of the heavy metals*, as of lead, copper, mercury, antimony, and iron, and arsenious and arsenic acids pass into the urine only in small amount. The excretion of lead salts is favored by the administration of potassic iodide. Prolonged use of salts of silver leads to a deposition of the metal in the glomeruli of the kidney, as well as in the rete Malpighii of the skin.

5. The acids appear as neutral salts.

6. Iodine appears as iodide, sulphur as a sulphate.

II. Organic Substances.

1. *Alcohol*, unless ingested in large amount, is generally completely oxidized, only traces appearing in the urine (HEUBACH, BINZ).

2. After long administration of *chloroform* the urine becomes possessed of strong reducing properties, and urochloralic acid is found in it. The sodium salt of this latter body crystallizes best, and has the formula $C_8H_{12}Cl_3NaO_7$; this acid appears to be a homologue of JAFFÉ'S

uronitrotoluic acid. *Chloral* also appears as urochloralic acid, the urine reducing sugar and polarizing to the left.

3. The *organic acids* are generally oxidized, and their alkaline salts render the urine alkaline; but gallic, pyrogallic, picric, and hippuric acids are very slightly changed; tannic appears as gallic acid, benzoic as hippuric.

4. The *amido-acids* go in part to form urea.

5. *Uric acid* appears as allantoin and urea, or as carbonic anhydride, oxalic acid, and urea.

6. The different *vegetable pigments*, and the *odorous principles* of valerian, assafœtida, castor, saffron, and turpentine appear in the urine.

7. The alkaloids, as quinine, morphia, strychnia, etc., pass over in great part unoxidized into the urine.

8. Of *aromatic bodies* such as the benzols and the like, some undergo simple oxidation, others reduction, and others again effect combinations with glycocin in the organism. *Benzol* appears as phenol and phenol sulphuric acid; *carbolic acid* as phenol sulphate, hydrochinon, and brenzcatechin. When phenol in any form is administered to a patient internally the whole amount may appear in the urine, sometimes causing it to assume a greenish brown color, especially in cases of poisoning; the color, however, is not proportional to the phenol present. An absorption of phenol takes place when applied to the uncut skin as well as after operations, a precipitate of coagulated albumen sometimes separating in the latter cases on distilling the urine. In passing through the organism it is capable of combining with sulphuric acid, forming an ethereal sulphate, which is afterwards eliminated by the urine as a potassic or sodic salt. In the urine, especially of herbivora, it is constantly present, and it is possible that it has its source here in the decomposition of tyrosin.

Glycocin, *leucin* and *sarcosin* appear as urea; *indol* as indican; *kreatin* as kreatinin; and *thein*, *theobromin*, *alloxantin*, and *allantoin* as urea. Most of these changes are analytical as well as synthetical, water being eliminated, and the requisite oxygen supplied from the blood. Blood containing hippuric acid passed through a pig's or dog's kidney, when the renal artery is tied, gives rise to benzoic acid, the change being due to a soluble ferment or "histozym" and not to the action of bacteria (SCHMIEDEBERG).

Methods for Detecting some of these Heterogeneous Elements
(*after* SALKOWSKI, *etc.*)

Potassic Iodide.—Add some drops of fuming nitric acid, then a few c.c. of chloroform, and shake well: the iodine is liberated and gives to the chloroform a violet tint.

Potassic Bromide.—If much is present, on heating the urine as in the case of the iodide, the chloroform will attain a yellow color.

Lithia.—Evaporate the urine to dryness and incinerate the residue on a platinum crucible; treat this with water and a drop or two of hydrochloric acid, and evaporate the extract obtained; this last residue is to be exhausted with strong alcohol, this diluted, and a clean platinum wire inserted in it and then placed in the colorless flame of a Bunsen lamp; a purple red color will be given to the flame, and on spectroscopic examination a carmine red line will be seen at B and a second between C and D.

Chloroform ($CHCl_3$).—Draw a stream of air through the moderately warmed urine, and then through a red-hot porcelain tube filled with fragments of porcelain, and finally through a set of Liebig's potash bulbs containing silver nitrate solution acidified with nitric acid. The chloroform is decomposed, and the hydrochloric acid gas generated is precipitated by the silver solution.

When the freshly-passed urine is boiled with an alcoholic potash solution and anilin a penetrating and characteristic smell is evolved:

$$CHCl_3 + 3KHO + C_6H_5NH_2 = 3H_2O + 3KCl + C_6H_5NC.$$

Chloroform may also be detected by proceeding as in the next paragraph.

Iodoform (CHI_3).—Distil the urine with steam until 50 c.c. have passed over; then mix the distillate with a little potash lye and shake it with ether in a tap funnel; the ethereal solution is evaporated to dryness, the residue treated with absolute alcohol, and the alcoholic solution tested by pouring it into a short test tube in the bottom of which is a very little alkali phenate; cautiously heat the mixture over a small flame, and in a few seconds a red deposit appears that dissolves with a crimson color in a few drops of dilute alcohol.

Phenol (C_6H_6O).—Acidulate the urine with sulphuric acid and distil; test the distillate with ferric chloride, which gives a blue color, or with bromine water, which gives a white crystalline precipitate of tribromophenol.

Salicylic Acid ($C_7H_6O_3$)—Shake about 30 c.c. of urine, that has been acidified with sulphuric acid, with an equal volume of ether; then decant the ether and treat it with a little ferric chloride, when a violet color appears. If much salicylic acid is present, the blue color may be obtained by testing the urine directly. The presence of free mineral acids in any quantity hinders or prevents the reaction; organic acids also hinder, but to a less extent. PAGLIANI therefore recommends the addition of the ferric chloride to the filtrate from the precipitate caused by lead acetate, and the gradual addition of sulphuric acid until the red color due to acetic acid just disappears, when the violet coloration due to salicylic acid will be seen.

Chrysophanic Acid ($C_{15}H_{10}O_4$) appears in the urine after its application to the skin, and also after the use of rhubarb and senna. The urine is generally of a strong brownish yellow color, and becomes a permanent purple red on the addition of caustic soda.

Santonin ($C_{15}H_{18}O_3$)—After its use a decomposition product is present in urine, owing to which this fluid generally acquires a yellow color, which is transitorily reddened by the addition of caustic soda or ammonia. To distinguish between the urine colored by it and by chrysophanic acid the following reactions will suffice:—

	Chrysophanic acid.	Santonin.
1.	*Alkalies* give a permanent red color.	A cherry or purple red color, which disappears after 24 hours. The tint is more of an orange after rhubarb or senna.
2.	*Alkaline carbonates* give a rapid red coloration.	The red color appears slowly and gradually.
3.	*Reducing agents* in the urine rendered *alkaline* remove the color.	The color remains.
4.	Precipitate with baryta water and filter: the filtrate is decolorized.	The color of the filtrate is not removed.

Quinine ($C_{20}H_{24}N_2O_2$).—Part appears in the urine unaltered, part as oxychinin (KERNER). The urine turns the polarized ray from 0·3 to 0·4 to the left. Add a few drops ammonia to the urine, shake well with some ether, remove the ether with a pipette, and evaporate the ethereal extract. The residue is to be dissolved in a little slightly acidified water and again precipitated with ammonia. Dissolve up this last residue with water and treat it first with chlorine water and then with ammonia: a green color is obtained; or if ferrocyanide of potassium is also added, a red color.

To detect very small quantities precipitate the urine with tannic acid and wash the precipitate by decantation; then treat it with caustic lime and evaporate to dryness; digest the residue with hot chloroform, and evaporate the chloroform extract. The quinine can be dissolved up from this last residue by means of acidulated water (PERSONNE).

Morphine ($C_{17}H_{19}NO_3$).—Only a part of the morphine taken into the stomach is absorbed, some being lost in the fæces; even when injected subcutaneously it is partly destroyed by the alkaline blood, so that only very minute traces, or at the most the products of its decomposition, can be detected in the urine (LANDSBERG). BÖRNTRAGER could not discover any morphine in the urine of a person who daily took it in large doses; but it always appeared there when it was subcutaneously injected. In a patient into whom a considerable amount was daily injected, one-fourth was found unaltered in the urine, and some was likewise discovered in the fæces (MARMÉ).

Evaporate the urine to a syrup, and extract it several times with absolute alcohol; evaporate this alcoholic extract to dryness, and dissolve the residue in a few drops acetic acid and water, shaking up the watery solution with warm amyl alcohol (70°) until it is colorless; then concentrate it over a water bath, and having rendered it strongly alkaline with ammonia shake it two or three times with hot amyl alcohol, which takes up the morphine and yields it on evaporation.

1. Dissolve a little in strong sulphuric acid, add a drop of water and a small fragment of red potassic chromate; a mahogany coloration is produced.
2. Heat the solution in sulphuric acid in an air bath at about 150° for 10 minutes or so, let it cool, and then add nitric acid, when a beautiful dark violet or blood red color is produced.

The *other alkaloids* are examined for in the same way. Test their action on frogs, and note if the pupils are dilated (*atropin*) or the muscles tetanized (*strychnin*), etc.

Lead, Silver, and Mercury.—In poisoning by *lead* the metal may be detected in the urine and all the organs of the body. In rabbits to which lead had been given in doses of 3 to 4 milligrams daily traces were found in the urine after the first day. The lead is best detected by treating the residue of the evaporated urine, or of any organic fluid, by first destroying all organic matters with hydrochloric acid and potassic chlorate, and testing the dissolved residue with sulphuretted hydrogen in an alkaline solution; or the lead can be separated by electrolysis, the solution, freed from organic matter and acidulated with hydrochloric acid, being placed in a bell jar closed below with parchment paper and floated in very dilute sulphuric acid. The positive electrode of a small battery lies on the parchment diaphragm and the negative electrode on the other side. The electrodes are platinum foil, and in 24 hours the lead deposited on the positive electrode is dissolved in boiling nitric acid, the solution evaporated to dryness, redissolved in water with the addition of caustic soda, and tested with hydric sulphide.

To detect *silver* evaporate the urine and destroy the organic matter in the residue by fusing it with potassic nitrate and sodic hydrate; extract with water, and dissolve what remains in nitric acid; this last solution is to be filtered, evaporated, dissolved in water, and precipitated with hydrochloric acid.

In the case of *mercury* the residue of the urine is freed from organic matters by means of potassic chlorate and hydrochloric acid, the filtrate subjected to electrolysis, the mercury being deposited on a gold electrode. The deposited mercury is then converted into iodide, the electrode being introduced into a glass tube, which is then drawn out into a capillary tube at one end and sealed at the other. On heating the bulb the mercury sublimes and passes into the capilliary portion of the tube. Cut off part of the bulbous portion of the tube and seal it up again after having enclosed a fragment of iodine; the iodine vapor penetrates the capillary tube and converts the mercurial sublimate into iodide. Or the urine may be diluted with water or a 2 per cent. sodic chloride solution, mixed with slaked lime, and some potash solution introduced, the whole being enclosed in a large flask. To the latter a U tube filled with glass wool moistened with silver nitrate is attached, and the whole then heated in a calcium chloride bath to 130° to 140°. The glass wool is next to be converted into iodide, as described above.

CHAPTER XXVI.

TABLE FOR THE EXAMINATION OF MORBID URINE.

1. *Quantity.*—Collect in a clear vessel the total urine passed in the 24 hours (normally 1,500 to 1,700 c.c. = 52 to 59 oz.)

2. *Density.*—Ascertain this with a urinometer (the normal is 1018 to 1025; to get it with any degree of accuracy, and so as to be really of service clinically, a sample taken from the whole mixed urine passed in the 24 hours should be tested).

To obtain approximately the solids in the 1,000 parts from the density multiply the last two numbers of the latter by 2 or 2·33 (TRAPP). [Normally 40 to 60 grams (617 to 925 grains) of solids in 1,000, or 4 to 6 per cent., of which urea = 370 grains, and inorganic salts, about the half of which are chlorides, = 300 to 350 grains.]

3. *Note the Color*, whether pale, yellow, brown, red, or black; the clearness or turbidity; the presence or absence of a *sediment;* and the *reaction* (of the fresh urine), whether acid, neutral, or alkaline. (If the litmus paper has been reddened and turns blue again on drying, the acid is free carbonic; while if the litmus has been colored blue but reddens again when the paper dries, or is gently heated on a slip of glass, the alkalinity is due to ammonium carbonate; but if it remains blue, then the alkalinity is due to fixed alkali.)

4. *Test for Albumen* by boiling the clear acid urine; if it is not already acid add a few drops of acetic acid, and then note if any precipitate appears on boiling. (When albumen is present the specific gravity is generally low and the urine pale in color.)

(*a*) If it is *white* and *disappears* on the addition of nitric acid it consists of earthy phosphates. (The nitric acid should not be added too sparingly.)

(*b*) If it is *white* and *does not disappear* on the addition of nitric acid it is albumen. But instead of appearing white it may be *green-colored*, from the presence of biliary pigment; or *reddish brown*, from the presence of blood.

Lay the test tube aside for 24 hours and then note the amount of the deposit. Roughly, if the precipitate is *insignificant*, the loss of albumen in the 24 hours is under 2 grams; if *moderate*, from 6 to 8 grams; if *considerable*, from 10 to 12 grams; while if *very large*, about 20 grams. If a more accurate determination is required see pp. 395–397.

To *confirm the presence of albumen*, particularly if it is in small amount, or if there is any doubt as to its existence in the urine, pour some *pure nitric acid* into a test jar, and allow the urine to flow slowly down the side of this vessel, held inclined at a considerable angle, and to spread itself out upon the nitric acid: then note the appearance of a *white cloud at the line of juncture of the two fluids.* Or a saturated solution of *picric acid* may be used in the same way.

Another confirmatory test is to boil the urine with a few drops of *Millon's reagent*, when an intense red coloration will be produced; or add to the urine a little *phosphotungstic acid*, which precipitates even *very* dilute solutions of albumen if a little time is given.

In slight cases of albuminuria the albumen may be absent from the urine passed before breakfast and present in considerable proportion after a large meal, such as dinner or breakfast. It is advisable, therefore, in cases of doubt or difficulty, to test samples of the urine of the early morning, of that passed after dinner, and of the urine voided at night.

5. *Test for Sugar.*—The urine is pale, abundant, and of high specific gravity (1030 to 1050) if sugar is present.

The urine should be *free from albumen:* if not, acidify it strongly with acetic acid, boil for some time, and separate the precipitate by filtration; or if *much pigment* is present filter the urine through animal charcoal.

(*a*) Add a little of the alkaline solution of bismuth (see p. 80) to the fresh urine and boil for a few minutes: a *brown or black* coloration or precipitate is indicative of sugar; a white precipitate is due merely to bismuthic oxide.

(*b*) Confirm the presence of sugar. (1) Add to it one-fourth its volume of caustic soda solution and then, drop by drop, a solution of cupric sulphate (1:10) until a blue solution is obtained; now heat, and a yellowish red precipitate is thrown down. Better results will be obtained by diluting a little Fehling's solution with water, boiling the mixture, then adding the urine gradually, heating after each addition. If sugar is present in not too small amount an orange or red precipitate makes its appearance. Also, for the sake of avoiding any possibility of reduction of the copper by other reducing bodies than sugar, it is advisable, if any uncertainty exists, to mix a little Fehling's solution with the urine and lay it aside for 12 to 24 hours: sugar alone, of any of the probable urinary constituents, effects the reduction in the cold.

6. *Test for Bile.* A. *Bile Pigment.*—The presence of albumen does not interfere with the pigment reactions. If, indeed, in the previous testing for albumen a greenish precipitate was obtained, then the presence of bile pigment is indicated. (*a*) Pour a little yellow nitric acid into a test tube, then inclining the test tube let the urine trickle

slowly down its side, so as to form a layer over the acid; at the point of contact a *green band first appears*, which spreads upwards, and is succeeded inferiorly by a blue, a reddish violet, and a yellow layer.

(*b*) Spread a drop of the urine upon a white plate and bring a drop of yellow nitric acid into the middle of this drop: a play of colors is produced, beginning with green and ending with red and yellow.

(*c*) A delicate plan is to filter the urine, dry the filter, and then allow a drop of yellow nitric acid to fall down the inside of the filter: the play of colors is well marked.

The presence of indican or the pigments of rhubarb, senna, santonin, etc., may lead to some difficulty. With the *indican*, however, the *appearance* of the *first green band*, so characteristic of bilirubin, is wanting, while the play of colors is absent with the other pigments.

(*d*) With only traces of pigment the above methods may fail; the following then is to be tried: Acidify the urine with acetic acid and shake well with a little chloroform; if pigment is present the chloroform assumes a yellow tint. Remove the chloroform with a pipette, allow a drop of it to evaporate on a microscope slide, and look for bilirubin crystals. Shake the rest of the chloroform extract with carbonate of soda, and an alkaline solution of the pigment is obtained, which is to be treated with nitric acid as in (*a*) or (*b*).

B. *Biliary Acids.*—(*a*) Add a few drops of cane sugar syrup to the urine, and then a little gum mucilage or a scraping of hard soap; shake for some time until a good froth is obtained; now incline the test tube and allow a drop or two of strong sulphuric acid to flow down into the froth; if the biliary acids are present a beautiful purple will show itself in the froth along the line of the sulphuric acid, either at once or after the side of the tube has been gently warmed.

(*b*) Dip a piece of filter paper into the urine in (*a*) after the addition of the cane sugar, and lay it aside to dry; then bring a drop of strong sulphuric acid in contact with it by means of a glass rod, and in a short time a violet red spot will appear,

(*c*) It is best, in case of doubt, to isolate the biliary acids as follows: Precipitate the urine with acetate of lead and a few drops of ammonia; collect the precipitate on a filter and wash it with water; next boil it with alcohol and filter hot; add some drops of sodic carbonate solution to the filtrate and evaporate to dryness. Extract the dry residue with boiling absolute alcohol, which is to be placed in a flask, and after having been evaporated to a small volume, ether added to it, the flask corked, well shaken, and laid aside; a resinous precipitate soon appears, which is to be separated and a watery solution of it tested as in (*a*) or (*b*).

7. *Test for Earthy Phosphates.*—Add to 15 to 20 c.c. urine in a test tube 5 to 15 drops of a solution (1 : 12) of carbonate of soda: the urine becomes opalescent or gives a precipitate. This indication is readily confirmed by adding a drop of nitric acid to another specimen of urine, and dipping into it a piece of ammonium molybdate paper, when the latter assumes a yellow color, which is more marked if the acidified urine has been previously boiled.

The precipitate that an alkaline or faintly acid urine may give on boiling, and which disappears on the addition of nitric acid, is due to earthy phosphates.

Approximately the amount may be determined by noting the character and amount of the precipitate with the sodic carbonate (BENECKE). If no cloudiness even is produced the phosphates are below 0·02 per cent.

	Per cent.
A slight opalescence	= 0·04 to 0·06
A stronger "	= 0·07 " 0·09
A marked "	= 0·10 " 0·12
A " turbidity	= 0·14 " 0·15
A moderate precipitate gradually appearing	= 0·16 " 0·18
A strong " appearing immediately	= 0·19 " 0·21
A precipitate occupying nearly the whole fluid	= 0·20 " 0·26
(*Normal amount*	= 0·06 " 0·08)

8. *Test for Uric Acid.*—Filter 200 c.c. urine, add 10 c.c. hydrochloric acid, and lay aside for 24 hours; a reddish or brownish yellow crystalline precipitate on the side of the tube. Collect these by decanting the urine and filtering. Place a few of the crystals thus obtained on a microscope slide, and dissolve them in a drop or two of caustic potash with the aid of heat; stretch a piece of linen thread through the drop and apply a cover glass; now let fall a few drops of hydrochloric or acetic acid at the side of the cover glass over the uncovered part of the linen thread; examine under the microscope in a few minutes, and note the appearance of transparent rhombic tables in the neighborhood of the thread.

The *murexid test* can also be applied, if required, to some of the crystals placed in a small porcelain capsule. Add a drop or two of nitric acid, warm, and evaporate at a gentle heat; moisten the reddish residue with ammonia, and it will become purple red, or with caustic potash, and a purple blue color will be produced.

If *excess of urates* is present the urine will not be clear, but it will become so on boiling, and will respond to the above tests.

9. *Test for Blood* if the urine is of a red, brown or brownish black color, and particularly if there is a reddish-colored deposit.

(*a*) Boil a little of the urine with some strong caustic potash, and let it stand for a short time: earthy phosphates will be precipitated, colored brown to a blood red and exhibiting marked dichroism with reflected light.

Urine containing chrysophanic acid or the pigments of rhubarb or senna gives a similar reaction; but there is no dichroism, and instead of the color of the precipitate being brightened by the action of mineral acids, as is the case with blood, it is somewhat darkened.

In cases of doubt apply the following tests in addition:—

(*b*) Boil the urine with acetic acid, collect the brownish red coagulum on a filter, wash it, and then warm it with a little alcohol acidified with sulphuric acid; a red or brownish red alcoholic solution is obtained, which is to be filtered and examined with a spectroscope; if sufficiently concentrated it will give the absorption bands of hæmatin, a dark band between C and D, and another lighter but broader band extending from midway between D and E to F, though sometimes this latter may appear as two bands instead of one.

(*c*) Add a little freshly prepared tincture of guaiacum to an equal volume of spirits of turpentine in a test tube, shake so as to form an emulsion, and pour the urine down the inside of the inclined test tube, so as to form a layer: if blood is present the resinous precipitate takes a blue color.

(*d*) A little of the deposit should be transferred to a slide and examined under the microscope. Look for the non-nucleated flattened discs, which may be more or less swollen and decolorized; then, if corpuscles are to be seen, and there is doubt as to their identity, irrigate with strong solution of *magenta*, which stains sporules and nuclei of epithelial cells; or with a solution of *eosin*, which imparts a rosy orange tint to the colored corpuscles.

(Where blood is present it is often of importance to get the patient to micturate into two clean vessels, so that the urine first passed may be examined separately from that passed later.)

10. *Test for Indican*—Mix 40 drops or so of urine with about 4 c.c. fuming hydrochloric acid; then agitate with some chloroform, which on settling to the bottom will be of a blue color if indican is present. Or warm the urine with twice its volume of nitric acid, and then shake with a little chloroform: a blue chloroform layer is obtained, that gives an absorption band between C and D.

11. *Test for Excess of Urea.*—The urine is of a deep color and a high specific gravity (1030 to 1040). Add to some urine in a large watch glass an equal volume of pure nitric acid, and float the glass on cold water. If the urea is in much excess crystals of nitrate of urea will make their appearance inside half an hour, or much earlier, according to the amount of urea present.

12. *Crystalline Constituents.*—Evaporate some urine to a thick syrup, place drops of this upon several glass slides, and apply thin cover glasses; after crystallization has gone on for some time examine under the microscope. Add a drop of acetic acid to one of the drops of the syrup and insert a filament of flax or silk therein: let this slide stand under cover for twelve to twenty-four hours, when it is to be examined.

CHAPTER XXVII.

URINARY SEDIMENTS OR DEPOSITS.

CERTAIN *extraneous* matters may be found in examining urinary deposits, and the student should in the first place make himself familiar with their appearance, so as not to mistake them for true urinary deposits. The most common of these *extraneous deposits* are fibres of cotton or flax, hairs of different animals, portions of feather, wool, oil. globules, granules of starch, pieces of vegetable tissue, splinters of wood, chalk, sand, etc.

It is always desirable to examine the deposits early, as some of them are liable to undergo preceptible changes in a comparatively short time.

A light cloudy deposit after the urine has stood a few hours is normal; it generally consists of epithelium or a little mucus from some part of the urinary tract. When the urine is turbid and acid on emission, the turbidity is due to the presence of pus, blood, or mucus; but if alkaline, to the presence of phosphates.

The deposits may be classified into organic and inorganic. The *organic* consist of epithelial cells, casts of the uriniferous tubules, pus, blood, oil globules, etc.; while the *inorganic* are such bodies as uric acid, urates, oxalates, phosphates, and carbonates, chiefly of the alkalies and alkaline earths, leucin, cystin, and tyrosin, etc.

Pus varies in appearance according to the reaction of the urine. When it is *acid* the pus tends to sink to the bottom of the vessel as an opaque, creamy, greenish yellow layer, diffusing readily on being agitated and subsiding again slowly and gelatinizing when mixed with an equal volume of caustic potash. When the urine is *alkaline* the pus is viscid and ropy, very tenacious and stringy, not diffusing readily on agitation, and generally mixed with earthy phosphates.

Mucus also tends to sink to the bottom of the vessel, and is very tenacious and ropy; earthy phosphates are frequently deposited.

The deposit should be allowed to settle, and the supernatent urine decanted, or the sediment removed by means of a pipette; and as a general rule portions of the deposit, if a copious one, *should be examined at different levels.* By using a conical glass sufficient deposit may be obtained for examination even from a small amount of urine.

The *character of the deposit* should then be noted—whether it is (1) *light, flocculent,* and *transparent*, consisting of mucus, epithelium, or other bodies, such as sarcinæ, spermatozoa, casts, etc., in small quantity: (2) *dense and opaque and of considerable bulk*, as *urate of soda*, forming a lateritious nut brown sediment; *phosphates*, urine usually alkaline; *pus*, forming a creamy deposit rendered glairy by potash: (3) *crystalline or granular*, occupying a small bulk at the sides or bottom of the vessel containing the urine, and colored or transparent, as *uric acid*, generally of a mahogany brown color; *blood* and other corpuscles and cells; *oxalate of lime* (seldom forming a deposit visible to the naked eye), *cystin*, etc. (BEALE).

We generally find that the deposit varies with the reaction of the urine; thus from an *acid* urine we may have a deposit of *urates, uric acid, tyrosin, or cystin*; from an *alkaline* urine, urate of ammonia, phosphate of lime or magnesia, triple phosphate, or carbonate of lime; and from a *nearly neutral* urine, oxalate of lime.

Removal of Deposit.—Plunge a pointed pipette, whose upper orifice is closed with the forefinger, into the deposit at the bottom of the vessel holding the urine, and then raise the forefinger slightly, upon which some of the deposit will enter; now press the forefinger tightly down and remove the pipette. If the deposit is present in but small amount, or if only a small quantity of urine can be obtained, the precaution should be adopted of attaching a piece of india rubber tubing provided with a clip to the upper end of the pipette. Then on removing the pipette from the urine lay it aside suspended for some time.

As a **preliminary examination** it is expedient to proceed as follows (after Robin):—

1. *Warm* a little of the deposit in a test tube with some of the urine itself: *urate of soda or ammonia* readily dissolves.

2. Add to a little of the deposit half its volume of *caustic potash: urates* are dissolved and a clear solution obtained; *pus* becomes transparent, glairy, and viscid; *phosphates* remain unchanged. If the deposit is rendered viscid without being cleared up, then pus and phosphates are probably both present.

3. If the deposit does not disappear when heated, add a few drops of *acetic acid: earthy phosphates* are dissolved.

4. If insoluble in acetic acid add to a fresh portion a few drops of *dilute hydrochloric acid*: a clear solution which gives a white precipitate when neutralized with *ammonia* probably indicates *oxalate of lime.*

5. If still insoluble, to a fresh portion add a few drops of *liquor ammoniæ:* if it dissolves, and the solution on evaporating leaves hexagonal crystals—*cystin.*

6. Also, if insoluble in the hydrochloric acid, test for uric acid by adding a drop or two of nitric acid to a little of the deposit on a small porcelain dish, heating to dryness over a spirit lamp, and adding a drop or two of ammonia: a purple coloration indicates *uric acid.*

7. Test the solubility of the deposit in *ether:* if soluble and the ethereal solution yields an oily residue, *fatty matter* is present. A partial clearing up occurs with *chylous urine.*

8. *Examine the deposit under the microscope*, and note whether it is crystalline or amorphous, or consists of rounded or organized particles.

(*a*) *Crystalline in Whole or in Part.*—*Uric acid* in lozenge-shaped crystals, but the form varies immensely. This is the most frequent form of deposit. Rhombs and rectangular prisms are the most common forms, and they are usually of a reddish yellow color. In case of doubt it is always advisable to dissolve a little of the deposit in a drop of potash on a slide, and then add excess of acetic acid: cover and examine in a couple of hours, when if uric acid is present small colorless rhombic crystals will be obtained. *Triple phosphate* occurs in stellate, feathery, or obliquely truncated triangular prisms, soluble in acetic acid; *phosphate of lime* in granules and occasionally in radiating crystals; *oxalate of lime* in octohedra or dumb-bells; cystin in rosette-like tables; *cholesterin* in rhombic plates.

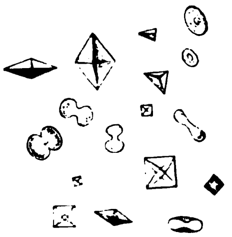


Fig. 35.—Oxalate of Lime Octohedra, Dumb-bells, and Ovoids.

(*b*) *Rounded or Amorphous Particles.*—*Oil globules* as spherical, very refractile bodies with dark borders; *chylous matter* as very minute fatty granules in an opaque and milky urine: fatty matter is generally in globules, chylous matter in a molecular condition. *Milk* can be detected by its characteristic globules, and by the urine clearing up after the addition of a few drops of acetic acid and ether, chylous urine clearing up on addition of ether alone. *Urate of soda or ammonia* occurs in amorphous form or in small rounded masses, and is readily soluble when heated; *phosphate of soda* is soluble in dilute acids: on adding acetic acid the phosphates and carbonates disappear, also the urates, but uric acid crystals will appear in the place of the latter.

(*c*) *Organized Particles.*—Corpuscles of mucus, pus, or blood, epithelial scales, casts, sarcinæ, etc. Irrigate with dilute acetic acid and stain with magenta. *Pus*, as we have seen, is rendered glairy by potash, and it is generally associated with crystals of triple phosphate. A little albumen also can be detected in the urine when pus is present, derived from different parts of the genito-urinary mucous membrane, even from the kidney itself; but to determine its exact seat of formation is difficult; some idea, however, may be gained by noting the character of the epithelial cells mixed with it, and the presence or absence of different crystals; thus pus from the bladder generally contains crystals of triple phosphate, but these are often absent if the pus comes from the pelvis of the kidney or the kidney itself. When *blood* is present the urine has generally a smoky tint, and if the urine is acid the deposit is brownish, but if alkaline the color is brighter and redder. The corpuscles will vary in their appearance according to the reaction and density of the urine; in dilute and alkaline urines they very soon lose their characters.

The opportunity may be taken here, before tabulating the different deposits, to examine one of these deposits in a little more detail. CYSTIN very occasionally occurs as a grayish crystalline deposit. Urine containing it is generally faintly acid, yellowish-green colored, and turbid when voided; the addition of acetic acid increases this turbidity by causing more cystin to be deposited. It occurs mostly in the urine of children or young adults, at times as much as 0·393 gram being excreted in the 24 hours, and is supposed to result from some derangement of the liver, the sulphates being generally increased at the same time unless much cystin is discharged, in which case the absolute amount of sulphuric acid is lessened. In some cases this cystinuria runs in families, and seems to be hereditary. In very small amount, it may be said, it has been regarded as a normal urinary constituent (LÖBISCH and EBSTEIN).

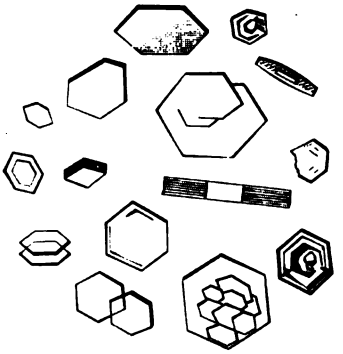


FIG. 36.—CRYSTALS OF CYSTIN.

Cystin forms transparent six-sided, or occasionally rhombohedral, plates. It is soluble in mineral acids, oxalic acid, and caustic alkalies, from which it is readily precipitated as a white powder, from the acid solutions by ammonium carbonate, and from the alkaline solutions by acetic acid; but it is insoluble in water, alcohol, and ether. Heated on platinum foil it burns with a greenish-blue flame, giving off a characteristic stinking, alliaceous, acid odor. On account of the sulphur present, of which it contains 26 per cent., if we boil a potash solution of cystin, containing some oxide of lead dissolved in it, a black precipitate of sulphide of lead will be formed; if boiled without the addition of the lead it gives off ammonia and some inflammable gas. Owing to the presence of sulphur also, if a small portion be heated on a piece of silver with some caustic soda a black stain of sulphide of silver is produced.

A little of the same boiled potash solution diluted with water gives with nitroprusside of potash a beautiful violet coloration.

Preparation.—(*a*) *To separate Cystin from a Calculus containing it.*—Boil the powdered calculus with caustic potash or a little carbonate of soda, and neutralize the hot solution with excess of acetic acid: the cystin separates as the liquid cools.

Or dissolve the calculus in ammonia, filter, and allow the ammoniacal solution to evaporate spontaneously. Cystin may be readily purified in this way by crystallizing it from its solution in ammonia.

(*b*) *From Urine containing it.*—Add to the urine $\frac{1}{10}$ its volume of dilute acetic acid (20 per cent.), and lay aside in a cool place: a sediment appears inside 24 hours, which is to be collected on a filter, washed with dilute acetic acid, and dried.

To Separate Cystin from Urine and Determine its Amount.—Add 20 c.c. dilute acetic acid (20 per cent.) to 500 c.c. of the urine; lay aside in a cool place, and collect the sediment after 24 hours in a weighed filter; wash the precipitate with dilute acetic acid, dry, and weigh it. The weighed filter with its contents is then to be treated with some drops of dilute hydrochloric acid, which dissolves out the cystin; dry the filter again and weigh: the difference in weight gives the cystin. From the acid filtrate the cystin can again be obtained by neutralizing with ammonium carbonate.

Cystin may readily be distinguished from urate of ammonia in urine by being insoluble, or nearly so, when the urine is heated, the urate dissolving readily. By its insolubility in acetic acid, the appearance of its crystals, and its ready solution in ammonia it is *distinguished from earthy phosphates;* and its sparing solubility in water *characterizes it at once from sodium chloride.*

Its *crystals may be preserved* in dilute acetic acid, or Canada balsam, or in gelatin and glycerin. They are *distinguished from similar-shaped crystals of uric acid* by treating them with ammonia and allowing the solution to evaporate, when the uric acid will remain as an amorphous residue of urate of ammonia, while the cystin will be deposited in its characteristic crystalline form.

Cystin is recognized (1) by the shape of its crystals; (2) by its ready solubility in caustic potash; (3) by the potash solution staining silver when heated on it; and (4) by giving a violet coloration with nitroprusside of potassium.

The deposit may further be examined chemically according to the methods given under calculi, or tested in succession with acetic acid and caustic potash according to the following tables (modified after MARAIS). Most of the chemical tests can be applied to the deposit on the slide, the precaution being taken of inserting a piece of thread under the cover glass to allow free entrance to the reagents.

A. Unorganized Deposits.

I. *Crystalline Bodies.*

	Action of acetic acid.	
1. Crystals large, generally isolated, transparent with sharp margins, and forming triangular prisms or many-sided rhombic combinations. Occasionally combined with these, and especially after the use of alkaline carbonates and in concentrated neutral or alkaline urine, magnesic phosphate [$Mg_3(PO_4)_2 + 17H_2O$] may appear as long, narrow, truncated tables.	Soluble.	***Ammoniaco-magnesian or triple phosphate*** [$MgNH_4PO_4 + 6H_2O$].

	Action of acetic acid.	
2. Crystals voluminous, but generally in groups, of a yellow or brown color, surface often furrowed or cracked, contours well marked (four-sided rhombic tables, six-sided plates, spindle-, barrel-, or dumb-bell-shaped crystals, etc.) In case of doubt dissolve in a drop or two of caustic potash, and reprecipitate in a crystalline form by the addition of a drop of hydrochloric acid: the crystals are colorless and lozenge-shaped.	Insoluble.	*Uric acid* [$C_5H_4N_4O_3$].
3. Crystals very small, isolated, very transparent, refracting light strongly, outline sharp and octohedral; occasionally arranged in rosettes, sometimes, however, occurring in small dumb-bells.	Insoluble.	*Oxalate of lime* [$CaC_2O_4+2H_2O$].
4. Yellowish-green globules with a striated, crystalline structure, soluble in ammonia and reprecipitated therefrom by excess of acetic acid in *long white needles*, that are generally grouped in radiating stars or bundles, or in brush-like masses.	Insoluble.	*Tyrosin* [$C_3H_7NSO_2$].
5. Appears frequently as white shining lamellæ, made up of small spherules, often as groups of spherical masses—balls or tubercles—exhibiting a radial striatión, the little spherules being made up of acicular crystals radiating from a common centre.	Insoluble.	*Leucin* [$C_6H_{13}NO_2$].
6. Pale or colorless, highly refractile, six-sided tables, soluble in hydrochloric acid and ammonia.	Insoluble.	*Cystin* [$C_3H_7NSO_2$].
7. Needles or rhombic prisms, insoluble in dilute hydrochloric acid, but soluble in warm alcohol (a very rare deposit).	Insoluble.	*Hippuric acid* [$C_9H_9NO_3$].

II. *Amorphous Bodies.*

	Action of acetic acid.	
1. Granules round or oval in shape, contour decided and dark, either isolated or united in groups of three or four, arranged in lines, etc.; or granules very pale, small, transparent, and difficult to distinguish, united in irregular flakes. (This body may also appear as wedge-shaped crystals with obliquely cut bases, and may be arranged in rosettes; the crystals may likewise form needles, or prisms collected into radiating clusters, etc.)	Soluble without evolution of gas.	*Phosphate of lime* [$Ca_3(PO_4)_2$].
2. Granules rounded, isolated, with concentric or radiated striæ, and more or less opaque and dark. (Only rarely found, and then generally accompanying the earthy phosphates in an alkaline urine; it may occasionally form imperfect dumb-bells.)	Soluble with evolution of bubbles of gas.	*Carbonate of lime* [$CaCO_3$].
3. Little reddish or yellowish granules, sometimes very small and disposed in a ramified series (recent sediments); sometimes more voluminous in the form of globules with black contour and yellow centre, united *en masse*, or else isolated and covered with points (old sediments). (Urate of ammonia is found	Soluble, with the appearance after a time of colorless rhombs of uric acid.	*Urates* [$C_5H_2(NH_4)_2N_4O_3$] [$C_5H_2Na_2N_4O_3$].

	Action of acetic acid.	
only in alkaline urine, the other urates generally in acid urine.)		
4. Very fine isolated granulations with molecular movement.	Insoluble.	***Molecular granulations.***
5. Rounded granulations of variable size and strong refracting power, soluble in a mixture of alcohol and ether, especially after the addition of a littie caustic soda.	Insoluble.	***Fatty particles.***

B. Organized Deposits.

I. *Of a Cellular, more or less Rounded Form.*

	Action of acetic acid.	
1. Globules circular with smooth and crenated margins, without nuclei, centre depressed, isolated, and often surrounded by threads of fibrin or mucus; the urine contains albumen.	Swollen and decolorized by dilute acetic acid; not stained by carmine.	***Colored corpuscles of the blood.***
2. Round or oval globules with faintly marked outlines, of a faint gray color, finely granular and nucleated; isolated or grouped, and often surrounded by strings of mucus. At first the *pus* corpuscles are separate, but they soon run together, so as to form a considerable gray or yellowish white sediment; and if the urine is alkaline the corpuscles appear much swollen up and transparent, often only their nuclei being visible.	Become pale, nuclei being brought into view, which are stained by carmine.	***Leucocytes*** **(mucus and pus corpuscles).**
3. Very small round or oval refracting globules, presenting brilliant nuclei or warty expansions on their surface; isolated or in strings.	Not affected; not stained by carmin, but the nuclei are colored yellow by iodine.	*Spores.*
4. Little vegetable organisms in the form of cubes (*sarcinæ*), or as cellular threads forming fungus growths (or thallus), often with fructifying spores (sugar fungus, *penicillium glaucum*).	—	*Fungi.*

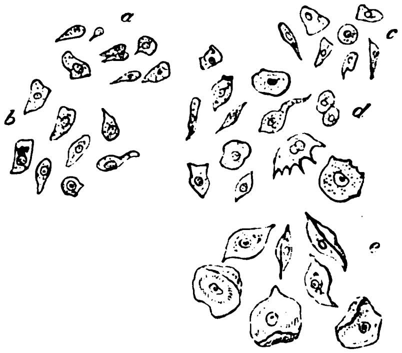


FIG. 37.—EPITHELIAL CELLS IN URINARY DEPOSITS.

Epithelium of different kinds found in urinary deposits: a, from ureter; *b,* from urethra; *c,* from pelvis of kidney; *d,* from bladder; *e,* from vagina.

	Action of acetic acid.	
5. Very small oval, hyaline, and highly refractile corpuscles, each furnished with a long and slender tail.	Not characteristically modified by reagents.	*Spermatozoa.*
6. Cells with thick walls, frequently tailed or spindle-shaped, often forming small brownish deposits in which blood corpuscles are numerous, and shreds of tissue, hæmatoidin crystals and rosettes of calcic oxalate crystals occasionally also present. The cells vary not only greatly in size, but likewise in shape, and pus corpuscles are not frequently combined with them (*cancer cells*). Broken-down cheesy masses with a large amount of amorphous granular débris and abundance of pus corpuscles (*tubercle*).	Elements rendered more distinct, particularly the nuclei.	*Cells and corpuscles of cancer and tubercle.*
7. Elements rounded, cylindrical, fusiform or polygonal, granular, generally nucleated, and never forming a voluminous layer. (Nucleated and elongated or polygonal epithelial scales may also show themselves.)	Rendered transparent, nuclei being brought into view which are stained by carmine, hæmatoxylin, or magenta.	*Epithelial cells*
(*a*) The *round* cells come from the kidney, the deep layer of the epithelium of the pelvis of the kidney, or of the male urethra, and are present in acute desquamative nephritis and acute pyelitis and urethritis. (*b*) The *conical* cells come chiefly from the pelvis of the kidneys, and (*c*) the *flattened* scales from the bladder or vagina. In jaundice the nuclei have a yellow color.		
8. In warm climates little oval plates with a sharp spine at one end have been found in cases of hæmaturia.	—	*Bilharzia hæmatobia.*

II. *Of a Cylindrical or Fusiform shape.*

	Action of acetic acid.	
1. Voluminous cylinders variable in length and appearance, often beset with blood corpuscles or with epithelial cells from the urinary tubules; to render them more evident irrigate with iodine or magenta solution, and at the same time limit the light by using a small aperture in the diaphragm of the microscope.	Rendered transparent.	*Urinary casts.*
(*a*) Colorless, flexible, slightly glistening, and coarsely granular, contour irregular, with nuclei and blood corpuscles here and there; dissolving in urine heated to 80°, shrinking in dilute acetic acid, and dissolving in strong acetic acid and in alkalies (*granular*).		
(*b*) Consist largely of epithelial cells embedded in a finely molecular, translucent mass; not soluble in water, and shrinking on boiling (*epithelial*).		

	Action of acetic acid.	
(*c*) Yellow, glistening, outlines regular and well defined; insoluble in water, lime water, or dilute acetic acid; soluble in strong acids and alkalies; and do not shrink in alcohol or tannic acid (*hyaline*).		
2. Very short and minute transparent rods or cylinders, in great numbers, and often presenting a molecular or undulatory movement.	Not modified by acetic acid, which, however, slackens or arrests their movements.	*Vibriones.*

III. *Flakes or Filaments.*

	Action of acetic acid.	
Filaments very fine and often intersecting.	(*a*) Not modified by acetic acid.	*Fungi.*
	(*b*) Rendered transparent by acetic acid, the fibrillary aspect disappearing and giving place to a swollen, transparent, amorphous mass, which again assumes its fibrillar appearance after the action of caustic potash.	*Clots of fibrin.*
	(*c*) Rendered more distinct by acetic acid, which gives it a striated or punctated aspect.	*Mucus.*

ACTION OF CAUSTIC POTASH (10 PER CENT.) ON DEPOSITS EXAMINED UNDER THE MICROSCOPE.

1. Deposit disappears:	*Urates*—the older the period of formation the slower the solution.
	Uric Acid—slow and progressive disappearance.
	Blood corpuscles—swell and dissolve.
	Leucocytes—become transparent and dissolve rapidly.
	Epithelial nuclei—clear up.
	Urinary casts " "
	Fibrin and mucus—the granules present are dissociated.
2. Deposit modified:	*Epitheliums*—the nuclei gradually disappear, the cell swelling up into a transparent vesicle with indistinct outline. Pavement epithelium resists the action longest.
3. Deposit not modified:	Triple phosphate.
	Phosphate, carbonate, and oxalate of lime.
	Spores, vibriones, bacteria—movements arrested.
	Spermatozoa.
	Vegetable filaments.

In the table preceding the last it will be seen that *after the action of acetic acid* the deposit disappears, as with the phosphates; is modified by being rendered transparent, etc. (*epithelia*, etc.); is not affected, as with uric acid, oxalate of lime, etc.; or new appearances present themselves, as crystals of uric acid, etc.

Hippuric acid may present itself in the form of long, rhomboidal, four-faced prisms, which may be confounded with the triple phosphate, but is distinguished by its insolubility in dilute acids and its solubility in warm alcohol. It is a very rare deposit, but it may present itself after the administration of benzoic or succinic acids and after the ingestion of large quantities of fruit, etc.

CHAPTER XXVIII.

PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS IN WHICH DIFFERENT SEDIMENTS OCCUR.

1. *Mucus and Epithelium* in blenorrhœa, catarrh of the urinary organs, etc.

2. *Pus* in suppuration in the urinary tract, as kidneys, ureters, bladder, urethra, etc.; also, in females, from uterine and vaginal discharges. If the cells are round and smooth and show double or treble nuclei readily on the action of acetic acid, the discharge is of a more or less laudable kind, and more likely to be produced by a simple catarrh, than if the action of acetic acid brings into view irregular or ill-defined nuclei.

3. *Phosphates.*—Especially in chronic diseases and in alkaline urine. The presence of the triple phosphate is not significant unless present in freshly voided urine; it then points to the occurrence of decompositions in the contents of the bladder and to the possible formation of stone. Crystalline phosphate of lime is said frequently to accompany the waste of tissue occurring in phthisis, diabetes, paralysis, etc. Amorphous phosphates, if persistent, indicate a low state of health, and may precede the formation of urinary calculi.

4. *Uric Acid and Urates.*—In acute fevers or exacerbations of chronic febrile conditions these are frequent. In a state of health a deposit often occurs after excessive bodily exertion, profuse sweating, excess of food, late hours, etc. A sediment of uric acid alone is very infrequent, but it has been met with in leukæmia. If the uric acid is deposited early in fresh urine it points to a uric acid diathesis, gravel, or the formation of a calculus. The occasional appearance of urates or of uric acid is of no importance; it is only their constant or frequent occurrence that indicates some error in one or more of the body functions. The deposit is frequently present in derangements of the digestive and hepatic functions. Very red urates are commonly associated with disease of the liver.

5. *Oxalate of Lime.*—SCHULTZEN states that there is a daily excretion of 0.1 gram of the oxalate, but it is increased after certain foods, drugs, or irregularities of diet; thus after sugar in excess, tomatoes, rhubarb, sorrel, gentian, valerian, etc.; also after excesses of carbonated drinks, such as champagne, seltzer, or soda water, etc., or of alkaline bicarbonates or alkaline salts of the vegetable acids; likewise in disturbed respiration, hindering absorption of oxygen, and thus leading to incomplete oxidation of certain of the non-nitrogenous constituents of the food, as in chronic pleurisy, tubercle of the lung, emphysema, and in dyspepsia, etc. It may show itself also in subacute rheumatism, diseases of the spinal cord, pityriasis, or spermatorrhœa; and MECKEL is of opinion that a deposition of the oxalate occurs in the mucus of the urinary tract under certain specific catarrhal conditions. A deposit of this body is frequently found associated with a series of nervous and dyspeptic symptoms indicating what is termed an oxalic acid diathesis, and constituting *oxaluria;* a modified form of this may also accompany many diseased conditions, as anæmia, cancer, and jaundice. Excess of acid in the system, moreover, is said to cause an increase in the discharge

of the oxalate, together with an excess of phosphate of lime—a condition frequently associated with flatulent dyspepsia.

In most of these diseases in which the oxalate is abundant there is probably more or less of an increased tissue metabolism, the urine at the same time containing an excess of urea, urates, and phosphoric acid.

The crystals of this body are soluble in a solution of acid sodic phosphate; after the urine has been passed this phosphate gradually diminishes, and accordingly the oxalate is deposited.

6. *Hippuric Acid.*—After the use of fruit, particularly cranberries, after the ingestion of benzoic acid, and in cases of diabetes and chorea.

7. *Tyrosin* indicates a great decomposition of protein substances, but at the same time the occurrence of some break in the continued downward metamorphosis, as in acute atrophy of the liver.

8. *Xanthin and Hypoxanthin* have been observed in leukæmia and after the use of sulphur baths.

9. *Cholesterin* has been found accompanying purulent discharges and in old inflammations of the kidney and its pelvis.

10. *Sarcinæ* are frequent in spinal cord affections, together with pus, phosphates, and ammonic carbonate (HELLER).

11. *Algæ and Fungi* appear particularly in diabetic urine.

CHAPTER XXIX.

URINARY CASTS.

In most cases of renal disease, such as congestion, inflammation, and the like, in which albumen makes its appearance in the urine, we also find casts of the uriniferous tubules, but the casts appear later than the albumen (OVERBECK). With the appearance of albumen in the urine a diseased condition of the epithelial lining of the urinary tubules sets in (SENATOR); but PERLS has obtained casts by compressing the renal veins, without any diseased condition of the epithelium showing itself; the occurrence, nevertheless, of a primary disease of the glomeruli in these cases is very probable (NUSSBAUM). Some of the fibrin-formers in the blood transude into the tubes, and there undergoing coagulation form casts of these tubes, and according to the condition and character of the tube at the time the appearance of the cast will vary. When the cast is dislodged and forced onwards it may carry with it the epithelium that lined the tube, or it may be a mould of the lumen of the tube alone; of course when the cells are discharged with the cast their character may often afford evidence of the condition of the kidney: thus, should the epithelium be degenerating, the altered cells will give evidence of this; so also the presence of blood corpuscles would indicate hemorrhage, and that of pus cells the existence of suppuration.

It is difficult, however, to understand how a cast of a convoluted tube could find its way into the urine if it has first to pass through the narrow-looped tube of HENLE, unless this had previously undergone dilatation, which is just possible; and, on the other hand, it does not appear probable that all the casts found in the urine come from the collecting tubes alone, although VIRCHOW was long of opinion that almost constantly, if not invariably, the casts were formed in these tubes. It is possible also that small casts may grow larger by successive deposition of new layers on their exterior.

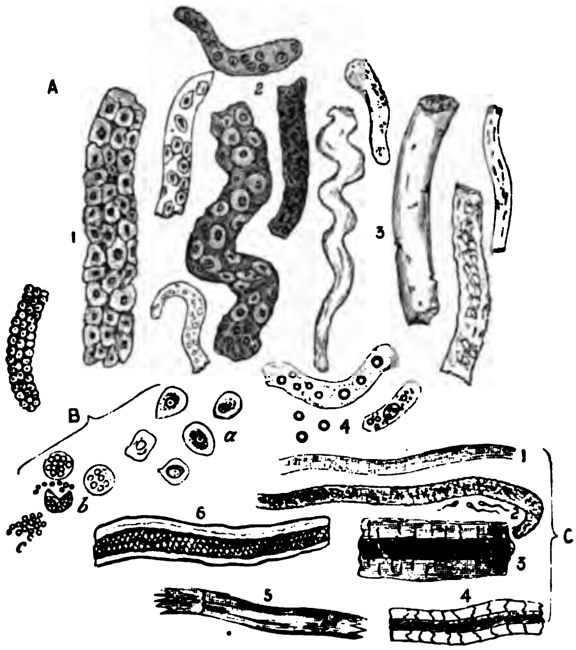


FIG. 38.—RENAL CASTS.

A. *Renal Casts.*—1. Epithelial casts: the middle one of the three is highly magnified; in that to the right the cells are scattered. 2. Granular casts: in the highest one there are blood corpuscles. 3. Hyaline casts of large and small diameter. 4. Fatty casts.
B. *Renal Cells.*—*a* in a normal and *b* in a state of fatty degeneration; *c*, free fatty granules.
C. Bodies that may be mistaken for casts: (1) mucus and (2) spermatic casts; (3) human hair; (4) woolen hair; (5) flax and (6) cotton fibres.

Classification of Casts.—Casts are of various kinds, of which the following are examples:—

I. 1. *Epithelial*, which indicate a desquamation of the urinary tubules.

2. *Hyaline* mostly long and narrow, and often so transparent and homogeneous as to escape observation unless the deposit has been treated with some iodine or magenta solution. Most of these hyaline casts swell up in pure water, and dissolve in it between 30° to 40° or at 60°. They are also soluble in 10 per cent. solutions of carbonate of soda or ammonia, in the mineral acids and the caustic alkalies; they shrink up in alcohol, and in solutions of tannic acid and the salts of the heavy metals; and when heated with Millon's reagent are colored violet. These may be the so-called *fibrin cylinders* or the *amyloid casts*, the latter of which glisten like wax and are perfectly homogeneous, but giving the blue reaction with iodine and sulphuric acid.

3. *Brownish yellow nucleated or granular casts* are generally wider in diameter than the hyaline casts, and often present fatty particles or degenerated epithelial cells in their interior. They do not swell up in water or in solution of sodium chloride or carbonate, nor shrink in alcohol or tannic acid; but they dissolve in hydrochloric (1 per cent.) and glacial acetic acid, and in alkaline solutions.

4. *Fatty Casts.*—The fatty particles may be studded over a transparent cast or collected in dark granular masses.

5. *Blood Casts* may appear, sometimes consisting almost entirely of blood corpuscles closely adherent and not much altered in appearance, or presenting a few scattered corpuscles along a fibrinous cast, or of corpuscles that have been as it were crushed together.

6. *Pus Casts* have also been described.

Reddish brown cylinders, made up of collections of urates or accumulations of bacteria, may make their appearance in urine.

II. *Cornil* admits four varieties of casts—*mucous*, *albuminous* or *hyaline*, *epithelial*, and *fibrinous*. (1) The *mucous* are pale, with ill-defined outline, and occasionally with a finely granular aspect; they are not stained by carmine. (2) The *albuminous or hyaline* possess well-marked outlines, and are often very long and twisted; they are soluble in caustic potash, insoluble in acetic acid, and colored by iodine and carmine. (3) The *epithelial* present swollen epithelial cells, that are generally very granular in appearance and infiltrated with fatty particles. (4) The *fibrinous* are finely striated or granular, often containing blood corpuscles and swelling up and becoming more hyaline in acetic acid.

III. Leube gives the following:—

1. *Blood casts*, consisting of coagulated blood.

2. *Hyaline casts*, mostly very small and colorless, and may be homogeneous, slightly striated, or molecular in appearance; they may contain leucocytes or epithelial cells, and are strongly colored by gentianin.

These are generally regarded as *fibrinous*, but more correctly they should be looked on as albuminoid in their nature, as they do not give the reactions of fibrin (Rovida). That they arise as the result of a coagulation of some kind, under the influence of dying leucocytes, there seems every reason to believe; and it may be possible that the fibrin has been metamorphosed in some way.

3. *Epithelial.*—(*a*) *Simple unaltered*—the cells distinct. (*b*) *Metamorphosed epithelium*—generally yellowish in color; the epithelial characters not always very evident; sometimes the appearance may be almost homogeneous.

They are generally broader than the hyaline casts, and may present in their interior more or less altered epithelial cells, fatty particles, micrococci, wandering cells, crystals, or precipitates of uric acid, etc.

The cells of the epithelial casts either break up into a finely granular mass, which later assumes a hyaline appearance, or they may swell up, run together, and become homogeneous at once.

Examination of Casts.—The specimen of urine should be laid aside in a small conical vessel and allowed to settle. With a pipette a little of the sediment is removed and examined under the microscope.

On account of the transparency of some of the casts the examination should be made, in case of doubt or difficulty, with a comparatively faint illumination through a small diaphragm, and sometimes it is advisable to stain the deposit with a little magenta; and where there is very little sediment it is often advantageous to allow the deposit to form in a pipette whose upper orifice is closed.

Pathology.—In many affections, such as fevers, severe inflammations, and the like, casts may appear in the urine, and probably result from some affection of the kidneys (congestion or the like) dependent upon the primary disease; but simple hyperæmia of the kidneys, it should be remembered, does not necessarily produce casts. Casts are generally present in albuminuria of renal origin; but in some forms of renal affection they are very scanty, and accordingly difficult of detection. Casts are found in (1) *acute nephritis*, either idiopathic or as a sequela of scarlatina, cholera, typhus, or variola; and in (2) *chronic Bright's disease.* Although, therefore, casts point to renal affection, we must not at once conclude the existence of Bright's disease. The irritation, for example, of a renal calculus may induce their formation; and in the urine of jaundice they may be found without any renal disease; indeed, it is possible for an occasional cast to be found in perfectly healthy urine.

Significance of Casts.—We must not expect to find in one case ephithelial casts alone, in another only granular casts, in another fatty casts, and in another large waxy casts, and so on; but several varieties may be met with in the same case, and the diagnosis must be founded upon the relative proportion of the different casts and of other deposits, as no one form can be regarded as pathognomonic of any particular disease of the kidneys. Thus the presence of uric acid crystals, blood corpuscles, and renal cells points to the case being *acute* while the occurrence of a number of oil casts renders it probable that the case is chronic (BEALE). Epithelial and blood casts as a general rule are typical of a disease of recent origin; transparent, large waxy casts, mixed with dark granular casts point to a chronic disease; and epithelium and casts containing much fat indicate fatty degeneration (ROBERTS).

Hyaline cylinders are found in all cases of *albuminuria*, whether of nervous or organic origin, and in *urine of fevers*, and they are especially frequent in *glomerular nephritis* and *contracted kidney*, although in this last epithelial casts are also present. The few casts that are met with in *amyloid kidney* are mostly hyaline; but as this latter condition is frequently associated with chronic inflammation other forms of casts may be present, as also leucocytes and blood corpuscles. In *chronic nephritis* especially the number of casts is particularly great, and there may be nucleated epithelial casts, or hyaline casts very broad and long, pale or dark yellow; and together with the casts blood corpuscles, fatty detritus, and degenerated fatty cells are present. In *acute croupous nephritis* the number of the casts is also considerable, and they may be of the hyaline or epithelial variety; they are associated with a copious deposit of blood corpuscles and epithelial cells from the kidney.

CHAPTER XXX.

CALCULI.

IN the following chapter, for the sake of convenience, biliary as well as urinary calculi, etc., will be considered. The substances that go to form these bodies are comparatively few in number. They are uric acid and urates, phosphate of lime and magnesia, oxalate and carbonate of lime, carbonate of magnesia, cholesterin, xanthin, cystin, biliary pigments, and coagula.

Occasionally calculi may consist entirely of one constituent, but it is more frequent to find two or more arranged in layers; but although most usually consisting of several constituents, one generally predominates, and the calculus is named accordingly. The combinations most commonly met with are uric acid and urates; uric acid, urates, and earthy phosphates; oxalate of lime and earthy phosphates; uric acid, urates and oxalate of lime; uric acid, urates, oxalate of lime, phosphate and carbonate of lime, and triple phosphate. These calculi are usually formed of layers, generally concentrically arranged around a nucleus of some kind, which may be a small calculus of renal origin, a clot of blood, some mucus, epithelium, or a foreign body; and in the case of uric acid calculi oxalate of lime very frequently forms the nucleus, while for other calculi the most frequent nucleus is uric acid itself.

In 80·9 per cent. urinary calculi the nucleus consists of uric acid or urates, in 8·6 per cent. of earthy phosphates, in 5·6 per cent. of calcium oxalate, in 3·3 per cent. of foreign bodies, and in 1·4 per cent. of cystin (Ultzmann).

The following is the frequency *per cent.* of the different urinary calculi (Fourcroy and Vauquelin):—

	Per cent.
Uric acid	25·0
Oxalate of lime	20·0
Urate of ammonia and earthy phosphates	11·7
Oxalate of lime and uric acid in layers	5·0
Oxalate of lime and earthy phosphates	2·5
Earthy phosphates	2·5
All other calculi, as cystin, xanthin, etc.	8·8

To see the concentric layers of a calculus divide it equatorially with a fine saw, then grind the cut surface on a hone with water, and having washed and dried it, apply a coat of varnish. In the case of small brittle calculi it is better to grind half the calculus away. No definite crystalline structure is usually to be seen unless occasionally on the surface.

Different Forms of Calculi, with their General Characters.—1. Most frequent urinary calculi are those consisting of *uric acid.* To other calculi they may be said roughly to stand in the proportion of two to three, or according to some authorities they form only one-fourth of all calculi. They are hard, generally of a flattened ovoid shape, and of all sizes from a pin's head up to a goose's egg; in color they are reddish or yellowish brown, smooth or slightly tuberculated on the surface, and crystalline or earthy in structure, consisting of a series of concentric layers. The calculus evolves an odor of burnt horn when heated on platinum foil, and is soluble in a dilute warm solution of caustic potash, from which it is precipitated by carbonic or acetic acid.

2. *Urates.*—These calculi usually contain soda, ammonia, and lime, and commonly oxalate of lime is also present.

(*a*) *Urate of ammonia* calculi are rare, being occasionally met with in young children. They are small, rounded, smooth or slightly tuberculated, and of a pale slate or clay color, but in the fresh state of a dull, opaque white.

(*b*) *Simple urates of soda and lime* are not found forming calculi of themselves, but they are often present with other bodies.

3. *Oxalate of lime* calculi are frequently met with, according to some authorities forming one-fifth of all calculi. They have most commonly a nucleus of uric acid or urate of lime, and are often of considerable size, brownish in color or of a dark olive or dirty purple tint (mulberry calculi), and possessing a very irregular and rugged surface, by which they can be recognized. They may also be met with in the form of small oval or rounded bodies, smooth and even polished on the exterior—the so-called *hemp-seed* calculi. The white crystalline variety is comparatively unfrequent. An oxalate stone with a phosphatic crust is a frequent form. Most mixed calculi contain more or less of the calcic oxalate.

The powdered calculus is insoluble in acetic acid, but readily soluble in dilute mineral acids, and precipitable therefrom by ammonia in excess.

These calculi may begin to be formed in the kidneys, and when they arrive in the bladder fresh oxalate may be deposited, or uric acid or phosphates, according to the condition of the urine.

4. *Calculi of the phosphates* are common. Less than 10 per cent. of all calculi have a nucleus of mixed phosphates, but they enter into the composition of at least 34 per cent. They are generally light in color and earthy in appearance. While the phosphates are very often deposited on other calculi it is rare to find uric acid, urates, or oxalate of lime deposited on the phosphates.

The mere presence of deposits of the earthy phosphates in the bladder, without the presence of some binding material like mucus or blood, is insufficient to give rise to a calculus (THUDICHUM).

(*a*) *Phosphate of lime* calculi are usually smooth on the surface, and their lamellæ are, as a rule, very regularly arranged, separating readily in thin crusts. They are almost infusible before the blowpipe. These calculi are easily soluble in nitric acid, and are precipitated in a gelatinous form from this solution by excess of ammonia, If the precipitate is dissolved in acetic acid the solution will give a yellowish white precipitate of phosphate of iron on the addition of a drop of ferric chloride, and a white precipitate of oxalate of lime on the addition of oxalate of ammonia.

These calculi are sometimes found in the kidney.

(*b*) *The triple or ammoniaco-magnesian phosphate* is somewhat rare as the sole constituent of a calculus, but it constitutes a large bulk of the mixed forms. It is of a drab or stone color and its surface is rough. It is easily soluble in hydrochloric acid and precipitated therefrom by neutralization with ammonia; boiling with caustic potash decomposes it, causing ammonia to be evolved and magnesia to be precipitated. This calculus swells up, gives off ammonia, becomes gray, and ultimately fuses in the blowpipe flame.

(*c*) *The fusible calculus* is a mixture of the triple phosphate and of the phosphate of lime, with a considerable admixture of mucus and organic matter. Next to uric acid it is the most common component of calculi. This calculus is generally oval or irregular in shape and resembles chalk in appearance and consistency, the hardness being nearly inversely proportional to the amount of triple phosphate present. It is easily fusible before the blowpipe without being consumed, a property that characterizes it and has given to it its name, evolving ammonia and watery vapor in the process, and leaving behind a mixture of calcic phosphate and magnesic pyrophosphate.

The powdered calculus is readily soluble in mineral acids, and is reprecipitated in stellate crystals by neutralizing with ammonia.

5. *Xanthin and cystin* calculi are extremely rare, particularly those of xanthin. The *xanthic calculus* ($C_5H_4N_4O_2$) is of a light or dark yellowish brown color, with occasional scattered white spots glistening like wax on friction. It is almost insoluble in water, alcohol, and ether, but soluble in alkalies and in warm hydrochloric acid; its solution in nitric acid leaves a bright reddish yellow residue on evaporation, which becomes a violet red (not a purple color, as in the case of uric acid) when treated with caustic potash. Xanthin solutions give a voluminous yellow precipitate with phosphomolybdic acid. Xanthin belongs to the uric acid group of bodies and is closely related to sarkin. It has also been found in very small amount in the spleen and liver and in muscle.

The *cystin calculus* is more or less transparent and waxy in appearance and crystalline in structure. Cystin calculi scarcely form 1 per cent.; they are generally small and may consist of pure cystin, when they are of a yellowish white or a pale greenish gray color, or of cystin combined with earthy phosphates, when they are dirty greenish blue or gray, or of a fawn brown. Cystin dissolves readily in ammonia, and the solution on evaporation leaves pure cystin in six-sided plates.

6. *Fibrinous calculi*, probably only the residues of altered blood clots, resemble yellow wax, and are soluble in acetic acid and caustic potash, but insoluble in water, alcohol, and ether.

7. Concretions of *blood* and of *fatty or saponaceous substance* (*urostealith*) are occasionally met with, as also calculi of *silica* and *carbonate of lime*. The carbonate of lime calculi are often found in the herbivora, and they may show themselves in great numbers in the kidneys of these animals. They are mostly white, but at times of a brown or violet color.

8. *Calculi of cholesterin*, generally mixed with more or less bilirubin and calcic phosphate, which are frequent in the gall bladder, have also been met with in the urinary bladder, in which case there is generally a layer of uric acid. But there is some doubt as to this form of calculus, and in one of the cases in which it was found a communication existed between the gall bladder and the urinary bladder through a patent urachus.

9. *Prostatic calculi.*—These are found in the follicles of the gland; they vary much in size, and are more or less rounded, with flattened sides, consisting of phosphate of lime with traces of carbonate of lime and organic matter.

10. Calculi may also be met with in the nasal fossæ, in the bronchial tubes, in the salivary glands, and in the intestines. These consist generally of mucus, epithelium, albumen, and earthy phosphates and carbonates, and sometimes also a little fat. Indigo has been found in a renal calculus (ORD).

Preliminary Examination of a Urinary Calculus.—Make a section through the centre and scrape some of the substance off one of the cut surfaces; sometimes it will be advisable to make independent analyses of the different layers, in which case, of course, portions of these layers will be collected. A. *Some of the powdered calculus is calcined on platinum foil.* The foil is heated to redness in the flame of a spirit lamp, and if a carbonized mass remains the red heat is to be continued until it disappears or forms a white ash. (1) If it is carbonized, then burns, and leaves no sensible residue, it most probably consists of *uric acid*, *urate of ammonia*, or such rare bodies as *cystin*, *xanthin*, *or fibrin.* (2) If it carbonizes at first, then burns, and leaves a sensible residue, it contains both organic and mineral constituents. Uric acid is the most frequent organic constituent; accordingly it should be looked for, and *some of the powdered calculus should be boiled with excess of water and filtered while hot.* Let the filtrate cool, and a deposit indicates urates of soda, lime, or potash; or evaporate the filtrate to the sixth of its volume, and uric acid and any urates present will be thrown down. Ammonia, lime, and magnesia may also be present, and these can be detected as follows: Boil a little of the filtrate with a few drops of caustic potash, and test the vapor given off with a rod moistened with hydrochloric acid; the presence of ammonia will be indicated by white fumes as well as by the smell. Then add to the rest of the filtrate some chloride of ammonium and carbonate of soda: a white precipitate indicates *lime;* filter, and add to the filtrate a little ammonia and sodic phosphate: a precipitate indicates *magnesia.*

The *residue insoluble in the boiling water* may contain phosphates or oxalates. Treat it with acetic acid and filter. The filtrate will contain the *earthy phosphates.*

Wash the residue and dissolve it in hydrochloric acid: if it dissolves without effervescence, and the solution supersaturated with ammonia gives a crystalline precipitate, *oxalate of lime* is present.

(3) If the calculus leaves a residue and undergoes little or no blackening under the heat, it is composed of inorganic substances, of which the most frequent are oxalate of lime and the phosphates.

B. *Digest some of the powdered calculus with caustic ammonia*, filter, and evaporate the filtrate, when, if *cystin* is present, microscopic hexagonal tables will be obtained, which dissolve in caustic potash, and when boiled with an alkaline solution of plumbic oxide give a deposit of lead sulphide.

C. *Dissolve a little of the calculus in nitric acid* and evaporate the solution to dryness: (*a*) a *yellow* residue rendered *orange* by caustic potash in the cold, but *violet* when heated, indicates *xanthin;* while (*b*) a *pink* residue which gives a *purple* color with ammonia marks *uric acid.*

Examination of a Biliary Calculus.—Biliary calculi (see *Bile*) may contain any of the following: cholesterin, pigments, biliary acids, mucus and epithelium, earthy salts, particularly carbonate of lime, and fats, like palmitin. Cholesterin is the most abundant ingredient, and often it occurs alone or combined with a variable amount of biliary pigment.

Analysis.—Powder the calculus, digest with hot alcohol, and filter: the filtrate contains fat and cholesterin; the latter will separate in crystals on the alcohol cooling, and the fat will be obtained by evaporating the alcoholic solution after the separation of the cholesterin. Some of the resinous products of the decomposition of bile may also be found with the fat. The residue left after the action of the alcohol is to be treated with dilute hydrochloric acid, which dissolves up the inorganic salts, and any effervescence will indicate the presence of carbonic acid. The undissolved residue consists of biliary pigments, which are to be tested with nitric acid.

The following method may be adopted: Digest a little of the powdered calculus with hot benzole and filter; this removes the cholesterin. Wash the residue with alcohol, then dry it and treat it with ether and a few drops of nitric acid; the fatty acids are thus removed. What is left on the filter is now washed with water, when the phosphates and nitrate of lime and magnesia are extracted. The final residue contains the biliary pigments mixed with a little earthy salts (THUDICHUM).

So far, then, as the action of heat is concerned we find that calculi may be arranged in *three classes*.

1. *Combustible*—uric acid, urate of ammonia, cystin, xanthin, cholesterin, biliary pigments, and coagula.

2. *Partially combustible*—urates of soda, potash and lime, and oxalate of lime.

3. *Incombustible*—inorganic constituents alone.

By means of the following table (SALKOWSKI) a calculus can be readily identified.

Powder the calculus finely and burn a little on platinum foil, noting whether it consumes away completely or only partially.

I. *Completely Combustible.*—Digest a little of the powder with dilute hydrochloric acid and warm gently.

a. The powder dissolves completely or nearly so: *cystin*, *xanthin*.

(1) Treat a little of the powdered calculus with ammonia and filter: on evaporating the filtrate cystin crystals are left behind.

Cystin stones are generally small, smooth. and yellow.

(2) Dissolve a little of the powdered calculus in a porcelain dish with nitric acid and evaporate: a bright yellow *xanthin* residue, that becomes violet red when treated with caustic potash.

Xanthin stones are very rare.

b. The powder dissolves imperfectly or not at all. Filter, and wash the insoluble residue.

(1) The *residue: uric acid.*

Confirm by the murexid test.

The stones are variable in size, moderately hard, and reddish yellow or brownish in color.

(2) The *filtrate* may contain ammonium chloride, xanthin, or cystin.

Try for ammonia by warming a little of the solution with sodic carbonate or hydrate, and testing the vapor by the smell, with red litmus, and with hydrochloric acid fumes.

Stones of urate of ammonia are mostly very friable and of a dirty grayish or yellowish white color.

A mixture of xanthin and cystin is rare.

II. *The calculus blackens, but is not combustible.* A slight blackening indicates the presence of an organic urinary constituent.

Digest some of the finely powdered calculus with dilute hydrochloric acid over a flame: a rapid escape of bubbles indicates carbonic anhydride.

a. Solution complete: absence of uric acid.

b. Solution incomplete. Filter: the *residue* may be uric acid or an albuminous body. The presence of uric acid is easily determined by the murexid reaction.

Render the *filtrate* weakly alkaline with ammonia, and let the test tube containing it stand in some cold water for a short time; then boil it and acidify with acetic acid: either a clear solution is obtained or a *white pulverulent precipitate*. (Yellowish white flocks occasionally present are due to ferric phosphate. By filtering them off, dissolving in hydrochloric acid, and testing the solution with potassic ferrocyanide a blue precipitate is obtained.)

c. The *white pulverulent precipitate*, insoluble in acetic acid, consists of *oxalate of lime*. Collect it on a filter, wash, dry, and ignite it on platinum foil: carbonate of lime is obtained, mixed with a little caustic lime; it has an alkaline reaction, and effervesces on the addition of hydrochloric acid.

d. The *filtrate* may contain phosphoric acid, lime, magnesia, potash, or soda.

(1) Test a portion with uranic solution or a drop of ferric chloride: a yellowish white precipitate indicates *phosphoric acid*.

(2) Treat the rest of the filtrate with oxalate of ammonia: a white precipitate indicates *lime*. Warm the fluid slightly and filter.

(j) To a part of the filtrate add a little sodic phosphate and ammonia: a crystalline precipitate, that forms gradually, is triple phosphate and indicates *magnesia*.

(ij) Examine another part of the filtrate for ammonia by boiling it with carbonate of soda and testing the vapor with litmus, etc.

(iij) Test a third part for soda and potash (although this is scarcely necessary) as follows: Evaporate to dryness, ignite, and then dissolve up the residue in water to which a few drops hydrochloric acid are added; now stir well in a white porcelain dish with a little platinic chloride, and a yellow crystalline precipate indicates *potash*. If the precipitate is transferred to a slide and examined under the microscope it will be seen that the crystals of the potash salt are octohedral and do not polarize, while the crystals of the sodic salt are acicular and do polarize. The flame also is to be examined spectroscopically, when a clean platinum wire moistened with the fluid is inserted in it; note also if the flame is bright yellow, or if it shows a violet tint when looked at through a piece of cobalt glass.

In phosphatic stones we generally find both lime and magnesia, although the crystalline phosphate of lime may occur alone; phosphatic stones are also more or less white and earthy-looking.

CHAPTER XXXI.

SYLLABUS OF PRACTICAL COURSE.

I. **Hydrocarbons.**

Starch.—1. Prepare a solution (p. 34).

2. Note the precipitation of this solution by tannic acid (p. 67).

3. Add a few drops of solution of iodine (p. 34) to a little of the starch solution, and a *blue* coloration will be produced; also irrigate the scrapings of

a sliced raw potato upon a glass slide with some of the same solution, and note, under a high power of the microscope, the dark blue staining of the starch granules.

4. Add to some gelatinous starchy mucilage a little lukewarm watery infusion of malt, and warm gently for a few minutes, when a thin fluid will be obtained containing sugar. Lay this aside, and test it afterwards for sugar (p. 66).

5. Starch is a colloid. Show this by means of a small dialyser (p. 66).

Dextrin.—1. Prepare by boiling a little starch paste with dilute sulphuric acid (p. 67).

2. Test with iodine solution, and note the *red* coloration obtained.

3. Note its precipitation from aqueous solutions by the addition respectively of alcohol, lime water, and a mixture of ammonia and basic acetate of lead, but not by the latter salt alone.

Glycogen.—1. Prepare by BRÜCKE's method (p. 69). The presence of glycogen in the liver has thus been demonstrated.

2. Show the *presence of sugar in the liver*, which has been derived from a conversion of the glycogen (p. 72).

3. Prepare the *liver ferment* (p. 73).

4. Test the glycogen with iodine solution, and note the reddish coloration (p. 73).

5. Test also with caustic potash and cupric sulphate, and note that the blue coloration does not disappear on boiling (p. 73).

6. Convert glycogen into sugar according to the methods given in paragraphs 3, 4, and 5, pp. 73, 74, and lay aside to be subsequently tested for sugar.

7. Precipitate a watery solution with acetate of lead.

Grape Sugar.—1. Prepare from cane sugar and honey (p. 77).

2. Boil a solution with half its volume of liquor potassæ, and note the brown tint acquired by the liquid.

3. Apply the copper test on p. 78.

4. Test with cupric sulphate and caustic potash (p. 78).

5. Boil a little of the solution with some alkaline solution of oxide of bismuth (p. 80, iij), and note the brown or black coloration due to the metallic reduction.

6. Apply the *fermentation test* according to method *a* or *d*, pp. 80, 81, and examine the growing yeast under the microscope (p. 82).

7. *Determine quantitatively* the sugar in a solution, or in diabetic urine—

(*a*) with a saccharimeter (p. 86);
(*b*) by FEHLING's method (p. 87);
(*c*) and by the differential density method (p. 90).

Fats.—1. Shake up a little oil in a test tube with some white of egg, and note the formation of an *emulsion*; then examine a drop of this under the microscope, when the oil will be seen to be broken up into small globules, varying in size and shape, which are maintained apart by their albuminous coatings.

2. Shake up a little oil with some caustic potash, and the oil will be *saponified*.

3. Apply the delicate test (p. 95, 1) for the presence of a fatty body.

II. Nitrogenous Bodies.

Albumens.—1. Prepare an albumen solution (p. 102).

2. Carefully perform test 1, p. 103.

3. Test with nitric acid as in 2, p. 103, using a very dilute albumen solution.

4. Test with picric acid in the same way.

5. Add some acetic acid to the albumen in solution and then a little potassic ferrocyanide.

6. Add some acetic acid and then an excess of a saturated solution of sodic chloride or sulphate.

In all the above precipitates will be obtained.

7. *Separation of Albumen from its Solutions.*—Mix equal parts of the albumen solution and of a solution of grape sugar; acidify the mixture with acetic acid and add an equal volume of a saturated solution of sodic sulphate; then boil for some time and filter. The sugar will be found in the filtrate.

Albuminates.—1. Prepare an *alkali albuminate* (p. 105, *a*, 1), and note that its solution is not coagulated by boiling.

2. Neutralize a solution of alkali albumen with acetic acid, and observe the precipitate that appears.

3. Boil a little solid alkali albumen with water; divide the solution into five portions, and proceed as follows:—

(*a*) Pass a current of carbonic acid gas through one of the specimens, and a precipitate will form.

(*b*) Saturate another with powdered magnesic sulphate, and a precipitate will likewise appear.

(*c*) Add alcohol to a third, and no precipitate will show itself.

(*d*) Neutralize a fourth specimen with dilute acetic acid, and a precipitate will be thrown down.

(*e*) Add a little sodic phosphate and a few drops of litmus solution to another specimen; then *neutralize* with dilute acetic acid, and it will be seen that no precipitate occurs until a considerable *excess* of the acid has been added.

4. Prepare an *acid albuminate* as in *b*, 1, p. 105; also by *gently* warming a dilute solution of albumen with a little dilute hydrochloric acid. The same result may often be readily obtained by rinsing out a test tube with nitric acid, and then pouring into it a little very dilute albumen solution; the whole is then to be very gently warmed for a few minutes.

(*a*) Boil a little of the albuminate thus obtained, and it will be seen that if the conversion has been complete no precipitate will appear.

(*b*) *Neutralize* a little of the solution with dilute caustic potash, and a precipitate will show itself, which will occur even after the addition of sodic phosphate.

Preparation of Certain Other Albumens.—1. Separate ***serum albumen*** from a little blood serum or hydrocele fluid by the addition of acetic acid drop by drop till a flocculent precipitate is obtained (p. 107).

2. Prepare *vitellin* by digesting some yolk of egg with water and ether so long as any yellow coloration is extracted. The residue is vitellin. Dissolve it in sodic chloride (10 per cent.), and precipitate it therefrom by adding an excess of water acidulated with a few drops of acetic acid (p. 109).

3. Separation of *paraglobulin* from the lens. Rub up a crystalline lens in a mortar with a little washed sand, then with some water, and filter: paraglobulin is present in the filtrate, and is thrown down by the passage of a current of carbonic acid gas, or by the cautious addition of dilute acetic acid (pp. 109, 245).

4. Prepare *myosin* by washing some finely divided muscle in water, and rubbing the washed mass in a mortar with ammonic chloride solution (12 per cent.); strain through muslin after 4 hours, and then filter, allowing the filtrate to fall drop by drop into a tall cylinder nearly full of distilled water. The myosin separates in small flocks (p. 110).

5. Prepare *fibrinoplastin* by diluting blood serum with ten times its volume of distilled water and passing a stream of carbonic acid gas through the diluted

fluid for half an hour (p. 111). Show also its precipitation by the addition of a little dilute acetic acid, or of an excess of powdered sodic chloride.

6. Prepare *fibrinogen* by diluting hydrocele fluid with ten volumes of water and then passing a current of carbonic acid gas through the diluted fluid for an hour or so (p. 112).

7. Dissolve separately the fibrinogen and fibrinoplastin thus prepared (the latter contains blood ferment mixed with it) in some dilute solution of sodic sulphate, and mix the solution together: *fibrin* will thus be generated.

8. Prepare *fibrin* by washing some blood clot (p. 114).

9. Prepare *casein* by diluting milk with ten times its volume of water, then acidifying with acetic acid, and subsequently passing a current of carbonic acid gas (p. 116).

10. Prepare *syntonin* by digesting for a few hours finely minced muscle in dilute hydrochloric acid ($\frac{1}{5}$ per cent.) and neutralizing the diluted filtrate therefrom with sodic carbonate (p. 117).

11. Test some purified amyloid substance with iodine, and with iodine and sulphuric acid; also with anilin violet (p. 120).

Gelatin.—1. Boil small pieces of skin, bone, or tendon in water for several hours, skim off the oil on the surface, then filter, and note that the filtrate sets on cooling (pp. 125 and 128).

2. Test portions of a hot-water gelatin solution with—

(*a*) mercuric chloride, tannic acid, and alcohol, and note the slimy precipitates obtained with each reagent;

(*b*) nitric acid, acetic acid, acetate of lead, alum, acetic acid and potassic ferrocyanide, and note the absence of all precipitation (p. 125).

Chondrin—To a solution apply the following tests:—

(*a*) Dilute nitric and acetic acids give precipitates.

(*b*) Tannic acid gives no precipitate.

(*c*) Alum gives a precipitate.

Mucin.—1. Prepare from tendon and bile as on p. 127.

2. Repeat the distinguishing tests for gelatin, chondrin, and mucin given on p. 128.

III. Some Albumen Derivatives.

Leucin and Tyrosin.—1. Prepare from shavings of horn or a mixture of fibrin and pancreas (pp. 130–132).

2. Add a drop of nitric acid to a few crystals of *leucin* on a piece of platinum foil, evaporate at a gentle heat; when cool, cover the colorless residue with a few drops of caustic soda, and heat again: a brownish yellow oily drop is obtained (p. 131).

A shining brownish yellow residue is obtained with crystals of *tyrosin*. which becomes brown on the addition of caustic soda, particularly when evaporated to dryness (p. 133).

3. Cover a few crystals of tyrosin in a small porcelain dish with a few drops of sulphuric acid; heat gently and lay aside for half an hour; then dilute with water. rub up with a little chalk, filter, and evaporate the filtrate to a small bulk: if necessary filter it again; the clear filtrate gives a violet color on the addition of a very little dilute solution of ferric chloride.

4. Examine under the microscope the crystals deposited from boiling watery and alcoholic solutions and from ammonia, and compare their appearance with the drawings given on pp. 130 and 132.

5. The urine of a patient suffering from acute yellow atrophy of the liver, malignant jaundice, severe typhus, or small-pox, if it is available, should be

examined according to the directions given on p. 131. The leucin will also be readily obtained by evaporating some of the urine to a syrup, which on cooling deposits the leucin in the form of circular yellowish discs; but if these are separated and then dissolved in boiling alcohol, the solution on cooling will deposit white shining crystalline plates which are insoluble in ether.

IV. The Digestive Juices and Digestion.

Saliva.—1. Collect some in a small beaker as in p. 143.

2. Boil a little saliva, and note the slight turbidity produced from the precipitation of albumen; show the albumen also by the nitric or picric acid test (pp. 103, 104, 2 and 3).

3. Place a drop of saliva upon a strip of filter paper that has been dried after immersion in an amber-colored solution of ferric chloride to which a few drops of hydrochloric acid have been added, and note the red stain produced. This is due to the sulphocyanide present in human saliva. The stain is removed by mercuric chloride, but not by hydrochloric acid (p. 158).

4. Prepare starch mucilage (p. 149).

5. Convert starch into sugar by the addition of saliva, as in p. 149, 2; then test for starch and sugar, and note the influence exerted by temperature, acids, etc., on the conversion (p. 149).

Gastric Juice.—1. Prepare some artificial juice from the mucous membrane of a pig's stomach (p. 143, *a* or *b*).

2. Make a glycerin extract of the dried and finely minced mucous membrane of the cardiac end of a pig's stomach (p. 147, 2), and precipitate the pepsin from this by the addition of absolute alcohol in excess.

3. Carefully repeat the experiments given on pp. 150, 151, and 152 (1 and 2), noting the gradual conversion of the albumen into peptone and the preliminary stage of an acid albumen; then apply the distinguishing peptone tests to the terminal digestive products (pp. 151, 152).

Pancreatic Juice.—1. Prepare the juice according to the directions given on p. 144, 3, *a*, mincing up a fresh pancreas, covering it with absolute alcohol, and rubbing up the dried mass with washed sand; the dilute acetic acid is then added, and, after mixing well together for 15 to 20 minutes, the whole is laid aside in a jar and covered with glycerin. Decant the glycerin extract in 3 days and filter.

2. Digest fragments of boiled fibrin in a one per cent. sodic carbonate solution to which a little of the above glycerin extract has been added (p. 152).

3. Prove a partial decomposition of the peptone formed into leucin and tyrosin (p. 153, 2, *a* and *b*).

4. Add a little of the glycerin extract to some starch mucilage and warm gently (p. 150); test for sugar after a few minutes.

5. Mince up some fresh pancreas very fine, and digest it with a little warm water, filter, and *neutralize* the filtrate, if necessary, with carbonate of soda.

(*a*) Rub up a little olive oil or melted lard with 3 or 4 times its volume of the watery infusion in a small warm mortar, and note the creamy emulsion formed.

(*b*) Shake up in a test tube a few drops of olive oil with a little of the same neutral infusion, and warm *gently*, taking care that the temperature does not rise very much. In about 5 minutes or so bring a drop from the bottom of the tube upon a piece of blue litmus paper, and note the red coloration produced, owing to the liberation of the fatty acid by the saponification that has occurred (p. 153).

V. Bile and Blood, etc.

Bile.—1. Repeat the two experiments given on pp. 153, 154, and show the emulsifying of oil by bile, and the more ready penetrability by oils of a membrane moistened with this fluid.

2. Apply **Pettenkofer**'s reaction to some bile in a test tube, as in 1, p. 177; also apply the modifications *b* and *d* given on the same page.

3. Place a drop of diluted bile on a white plate, and allow a drop of yellow nitric acid to flow into it; at the line of contact a series of colored bands will make their appearance.

4. Examine with the spectroscope some fresh bile, some altered bile, and a filtered dilute hydrochloric acid extract of bile (p. 178, 3).

5. Prepare the *biliary acids* according to method 1, p. 180.

6. The **Pettenkofer** reaction should be repeated with some of the biliary salts prepared as above (p. 182).

7. Prepare *bilirubin* from biliary calculi according to method 1, p. 185; or, if dog's bile is procurable, according to method 3, p. 185.

8. Dissolve a little bilirubin in ammonia; to the solution thus formed add nitric acid drop by drop, and note the marked play of colors (p. 185), the final product of the reaction being choletelin.

9. Dissolve a little bilirubin in caustic soda contained in a small flask, add some fragments of sodium amalgam, and lay aside loosely corked for 2 or 3 days. Note the gradual disappearance of color. Decant after a time, and to the decanted liquid add hydrochloric acid drop by drop until a brownish flocculent precipitate of *hydrobilirubin* makes its appearance (p. 186).

10. Spread out a thin layer of a caustic soda solution of bilirubin upon a plate, and expose it to the air; the color will soon become intensely green, owing to the formation of *biliverdin*.

11. Separate *cholesterin* from some powdered pale biliary calculus by boiling it with some spirit to which a few drops of caustic potash have been added; filter hot, and when the filtrate cools crystals of cholesterin will be deposited. Note that these crystals are easily soluble in ether.

(*a*) Place a few crystals on a glass slide, add to them a drop of sulphuric acid, mix with a glass rod, and heat the slide gently; apply a cover glass, and note under the microscope the carmine tinting of the edges of the crystals (p. 188).

(*b*) Dissolve some crystals in a little chloroform and mix with an equal volume of strong sulphuric acid, when a red solution is obtained, which rapidly changes color, becoming blue, green, and finally yellow (p. 188).

(*c*) Cover a few crystals lying in a small porcelain dish with a drop of nitric acid, and evaporate to dryness at a gentle heat: on touching the yellow residue with ammonia a deep red color is produced, which is not altered by the addition of caustic potash.

Blood.—1. Examine blood under a high power of the microscope, and carefully note the appearance of the *corpuscles*. This should be done with human blood as well as with the blood of a frog, a bird, and a dog or cat; the blood also should be examined alone and after the addition of sodic chloride solution (0·75 per cent.)

2. Prepare crystals of *hæmoglobin* from the blood of a guinea pig and of a rat (1 and 2, pp. 199, 200), and examine them microscopically (p. 202).

3. Prepare crystals of *hæmin* as in method 1, pp. 211, 220, and examine them under a high power.

4. Apply the ozone or guaiacum test for hæmoglobin (pp. 204, 218).

5. Add a few drops of blood to a small test tube nearly filled with water, and examine with the spectroscope: the two absorption bands between D and E will be seen (pp. 203, 205).

6. Add some reducing agent to the diluted blood in the small test tube, and rapidly examine again, when it will be found that in place of the two stripes a single broad band is to be seen, due to reduced hæmoglobin (pp. 205, 203).

7. Now try to get the oxyhæmoglobin bands by spectroscopically examining in a dark room the rosy light that passes between two of the fingers held together in front of a bright light; and, when this has been accomplished, look in the same way for the single band of reduced hæmoglobin after both fingers have had the circulation in them arrested by the application of an elastic ligature at their bases (p. 217).

8. Take a piece of rag that has been stained with blood, scrape the spot, and digest the scrapings in water to which a little ammonia has been added; examine the colored solution thus obtained with the spectroscope, and look for the absorption bands of oxyhæmoglobin (p. 203); then add a little reducing reagent and look for the single band of reduced hæmoglobin; note also that by shaking the red solution in the air the two bands reappear.

If much ammonia is now added to some of this colored solution a broad band of alkaline hæmatin will generally be found between C and D.

Next add glacial acetic acid in excess to the rest of the red solution, and transfer the mixture to a small stoppered bottle, where it is to be well shaken with an equal volume of ether. The ether soon separates on standing, and it will have a reddish brown color; it is then to be decanted into a small glass vessel with parallel walls and examined with the spectroscope (pp. 209, 218, and 219).

9. Leave a blood-stained rag in water for a couple of hours, and note that the dingy red solution obtained gives a dirty red coagulum when boiled and on the addition of nitric acid, also that with dilute hydrochloric acid and potassic ferrocyanide a bluish precipitate appears (p. 217). Leave another piece of stained rag in some water in a test tube for an hour or so; then add a few drops of ammonia and boil, when a dirty gray turbidity is produced, which disappears on the addition of a drop or two of caustic potash, a solution, green by transmitted and red by reflected light, remaining behind.

10. Repeat the six tests for blood given on p. 220 with a single spot of blood on a piece of linen rag.

Lymph and Chyle.—1. Examine microscopically some lymph obtained by plunging a capillary glass tube into one of the dorsal lymph sacs of a frog. Note the character of the corpuscles, etc. (p. 229).

2. Examine in the same way some of the chyle obtained from the intestine of a rabbit. Note the corpuscles and the molecular basis, and then irrigate with ether and caustic potash (p. 231).

VI. Certain other Secretions and Tissues.

Pus and Mucus.—1. Examine drops of both fluids under a high power, noting the corpuscles, free molecules, and fatty granules, etc. After having looked at them without the addition of any reagent, examine them in sodic chloride solution (¾ per cent.), and then irrigate with dilute acetic acid. In the case of the mucus threads of mucin will be seen (p. 236).

Bone.—The practical exercises commencing at p. 253 should now be performed, with the exception of the quantitative analysis.

Muscle.—1. A piece of living muscle from an animal just killed is to be compared with a piece of muscle that has entered into a state of rigor (p. 259).

2. Prepare kreatin from Liebig's extract of meat by process 2, p. 262. The crystals, when separated, are to be examined microscopically and their characters noted (p. 261).

3. With a watery extract of Liebig's extract of meat make the analysis given on p. 269, C.

Milk.—Repeat the tests given on pp. 316, 317 (1, 2, 3, 4, and 6,), first examining a drop of milk under a high power of the microscope, then taking the specific gravity, separating the casein and butter, and detecting the sugar; also determining the percentage of solids (p. 317, 1), and making an approximative determination of the cream present (p. 317, 2, ij).

VII. Urine.

1. The *reactions and characteristics of normal urine* are to be carefully noted in detail (pp. 333–336).

2. Repeat the *tests* (1–5, 7, and 8) *for urea* given on pp. 339, 340.

3. *Determine the urea in urine quantitatively* by Liebig's mercuric nitrate method, as detailed on pp. 344–347, and also by its conversion into nitrogen gas with Russell and West's or Simpson's apparatus (pp. 352–354).

4. Perform the first four tests given for *uric acid* on pp. 357, 358.

5. Determine approximately the *uric acid* in a specimen of urine by adding a little hydrochloric acid to it and laying aside for 24 hours (p. 358).

6. Test for *indican* by acidifying strongly with hydrochloric acid and then shaking up with a little chloroform (p. 373).

7. *Determine the sodic chloride* present in urine by Mohr's or Folhard's process (pp. 379, 380).

8. *Separate the organic and inorganic sulphates* present in urine by method 2 on pp. 382, 383.

9. *Determine the sulphates of urine volumetrically* by means of standard baric chloride (p. 383).

10. Examine a urinary *deposit containing uric acid, urates, and phosphates:* warm part of it up with a little of the urine, when the urates will disappear, causing a partial clearing up; now add some acetic acid, and the phosphates will dissolve; filter, and the residual uric acid will dissolve on the addition of caustic potash. Some of the deposit should be further examined under the microscope, when the yellow, brown, or reddish-colored crystals of uric acid will be seen scattered amidst the rhomboidal or triangular prisms of the phosphates and the abundant amorphous granules of the urates (pp. 384, 385).

11. *Separate the phosphates* from urine by magnesia mixture (p. 387), and by baryta mixture (p. 347).

12. *Determine the amount of phosphoric acid* by means of standard uranic solution (p. 387), and also approximately by Teissier's method (389, III.)

13. Test some *albuminous urine* by boiling and by nitric and picric acid (pp. 393–395).

14. Detect the presence of *blood* in bloody urine by the tests on pp. 401–403.

15. Test some diabetic urine for *sugar* by the first four methods given on pp. 405, 406.

16. *Estimate the sugar* in a specimen of diabetic urine by Fehling's method (p. 87), and also by Bouchardat's approximative method (409, III.)

17. Test for *biliary acids and pigment* in a specimen of biliary urine (pp. 411–414).

18. Examine a specimen of morbid urine according to the table given on pp. 423–426.

VIII. **Urinary Deposits and Calculi.**

Deposits.—1. Examine a little of the deposit according to the method given on p. 428, confirming the results obtained by the tables on pp. 430–434.

2. Note the action of caustic potash on the deposit when examined microscopically (p. 434).

3. In specimens of albuminous urine *casts* are to be looked for under the microscope (p. 439).

Calculi.—Several specimens of powdered calculi are to be examined according to the method given on p. 443, and the results obtained confirmed by the table given on p. 444.

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